Modern Materia Medica

FOR

PHARMACISTS, MEDICAL MEN, AND STUDENTS,

BY

H. HELBING, F.C.S.

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INTRODUCTION.

SYNTHETICAL remedies have become one of the distinctive features of our time. The zeal and untiring energy of the old alchemists in their search for the philosopher's stone and the elixir of life' are reproduced to-day in the eager quest of their scientific descendants for artificial alkaloids.

Since the time when the modern chemist first became fired with the ambition to win fame and wealth at one stroke by the synthesis of quinine, the number of remedies turned out yearly from the chemical laboratory has gone on steadily increasing, and if the original aim of the work is still unaccomplished—as the process of M.M. Grimaux and Arnaud is but a partial solution of the problem—yet among the very considerable number of compounds produced, some have been found capable of replacing the natural alkaloid in many cases, while in others they seem to be even superior to it in therapeutical activity, reliability or safety.

Not a few of the medical agents, thus, as it were, created, have won the favour of the medical profession sufficiently to secure them a place in the chief European Pharmacopœias. But there is a much larger number, the members of which are still on trial—passing through their period of probation—and of these of course there is no official recognition. Nevertheless their importance is, in some instances, not at all inferior to that of the pharmacopœial compounds, and hence they are more or less generally used by the medical man, and cannot be ignored by the pharmacist who desires to keep abreast of the times.

Naturally, however, the literature of substances produced at different times by various manufacturers and examined by pharmacologists and chemists in all parts of Europe and of the civilised world is widely scattered, and not easy to come at. For this and other more or less potent reasons it has become exceedingly difficult, if not impossible, for the busy medical man or pharmacist to maintain his acquaintance with the properties and uses of the therapeutical novelties continually being brought under his notice in the scientific press of the country.

To be *au courant* with the growth of synthetical materia medica, however desirable, is, however, not all that the followers of medicine and pharmacy require. Information of this kind, if it is to be of practical service, must be in such a form as to be available for ready and more or less frequent reference.

It is the aim of the following pages to supply the want generally felt in this country of full and comprehensive details as to the constitution, methods of preparation, tests and medicinal application of new remedies. The requirements not only of the pharmacist, but also of the therapeutist and general practitioner, have been kept in mind; while further, the work is designed to rank as a text book for purposes of study. It would, perhaps, be well to add that in dealing with the "medicinal uses" of each compound it has been a constant endeavour to indicate its therapeutical importance, where possible, rather by a careful balancing of the whole literature of the subject than by a detailed quotation of individual experiences and conclusions.

Every monograph has been carefully revised and extended, where necessary, in order to make the volume representative of the progess of synthetical remedies down to the date of issue. It is believed that the practical value of the work to all classes of readers will be enhanced by the appendix, the various tables, and not less by the index, with which equal care has been taken.

LONDON: June, 1891.

CONTENTS.

Modern Materia Medica.

ACETANILIDE.

(Antifebrin; Phenylacetamide).

One of the simplest synthetical compounds of the "new remedy" era. Is now official under the name "Acetanilidum."

Preparation.—By the prolonged interaction of pure aniline (boiling point 184°—185° C.) and glacial acetic acid at a high temperature, fractional distillation (collecting what passes over at 295° C.) and re-crystallisation from boiling water. The reaction may be thus represented:—

$$C_6H_5NH_2 + CH_3COOH = C_6H_5NH.CH_3CO + H_2O.$$

It should be observed that simple as this process appears upon paper it is practically very difficult to obtain a pure product even with special plant and large experience.

Physical and Chemical Properties.—When pure, acetanilide forms lustrous rhombic tables without colour or odour, but with a peculiar greasy feel and a slight burning taste. It requires nearly 200 parts of water at 15° C. for solution, but only 18 of the same solvent at 100° C. (forming neutral solutions); soluble in alcohol (1 : 3½), readily in ether and in chloroform. According to the B.P. Addendum the crystals should melt at 112.8° C. (235° F.). When melted it forms a clear, colourless liquid, and

distils unchanged at 295° C. By Ritsert the melting point of pure acetanilide is said to be 114° C., but the question is still an open one. By continued contact with hydrochloric acid or potash at high temperatures it splits up into its components.

Acetanilide is identified in the additions to the B.P. 1885 by the development of the odour of phenyl-isonitrile when heated with solution of potash and a few drops of chloroform. Other characteristic reactions are the formation of a yellow-colouring substance with a beautiful moss-green fluorescence (flavaniline, $C_{16}H_{14}N_2$) when heated for some time with an equal weight of zinc chloride. Six grains boiled for a few minutes with 1 fl. drm. of hydrochloric acid form a clear solution, which, on the addition of 3 fl. drms. of water and 4 drops of carbolic acid previously dissolved in ½ fl. drm. of solution of chlorinated lime, assumes a turbid, dirty-red colour, and, on the further addition of excess of ammonia, an indigo blue (indophenol).

Free acetic acid is detected by the litmus reaction, acetone by ferric chloride, which must not affect the *cocl*, aqueous solution, and aniline by solution of 15 grains in 1 fl. oz. of hot water (the solution is turbid if aniline be present, and smells of the latter). General impurities are detected by determination of the melting point and ignition on platinum foil (no residue should be left).

Ritsert states that a boiling, aqueous solution should not decolorise 1 drop of solution of permanganate of potassium.

Medicinal Uses.—This compound was first introduced into medicine under the name antifebrin, in 1887, as an antipyretic. Internally it is given in 3 to 8 grains doses, preferably as powder, in wafers, capsules, &c., and chiefly as an analgesic in neuralgic and rheumatic affections. In 5 grain doses it has been warmly recommended in labor where the pains are weak and irregular.

Primarily it found application further as an antipyretic in typhus, pneumonia, pleuritis, puerperal fever, and phthisis, but its use in these directions is now restricted. The remedy has been stigmatised as dangerous, if not poisonous, and the literature relative thereto is copious and imposing, but it seems probable that the prejudicial effects have been in many cases due to impurities. Externally, it has been employed as an antiseptic in the treatment of wounds, but cannot be recommended for that purpose.

Acetanilide has been sometimes found as an admixture in other remedies, such as phenacetin and antipyrin (*v.* under these names); its detection is a matter of great importance, not only on account of the difference in commercial value but also because of the smallness of its dose as compared with that of the substances so contaminated.

Mention may here be made of a derivative of acetanilide which was introduced under the names *Monobromacetanilide*, *Parabromacetanilide*, *Asepsin*, and *Antisepsin*, as an anodyne, analgesic and antiseptic. It appears to have been successfully employed in a few cases of neuralgias, but its literature is meagre. *Antinervin* and *Salbromalid* are names for what is said to be a mixture of bromacetanilide and salicylanilide.

Under the name *Antikamnia* a substance has been recently introduced by an American firm. It occurs as a fine white powder, seen under the microscope to be a mixture of bodies of different crystalline form, determined by analysis to be sodium bi-carbonate, acetanilide and caffeine (Goldmann and Hoffmann). 100 parts of the air-dried mixture were found to be made up of 22.2 parts of the bi-carbonate, 67.4 of acetanilide and 9.8 of the alkaloid, so that the proportions adopted originally are probably 20, 70 and 10 respectively.

AMYLENE HYDRATE.

(Dimethylethylcarbinol; Tertiary Amyl Alcohol).

$(CH_3)_2\ C_2H_5\ COH.$

One of the eight possible alcohols with the general formula $C_5H_{12}O$. First prepared by Wurtz, and identified later by Flavytzky and Osipoff.

Preparation.—By the action of sulphuric acid upon amylene at a low temperature, separation of the amylenesulphuric acid, dilution with ice-cold water, filtration, neutralisation (with chalk or soda) and distillation. The distillate is freed from water by potash and fractionated, the fraction which passes over between 100° and 102.5°C. being collected.

Physical and Chemical Properties.—Amylene hydrate is a limpid, colourless, hygroscopic liquid, with a peculiar penetrating ethereal odour, which reminds of camphor and peppermint. Its specific gravity is 0.81, and when pure it boils at 102.5°C. In a mixture of salt and ice it solidifies at -12.5°C. to long acicular cystals, which melt at -12°C. Amylene hydrate dissolves in 8 parts of water at 15°C., the solution becoming turbid when warmed. It is miscible in all proportions with alcohol, ether and chloroform.

By oxidation with chromic acid it splits up into acetic acid and acetone.

Amylene hydrate is tested by determination of the physical factors. The liquid must not affect blue litmus (sulphuric acid) nor decolourise weak potassium permanganate solution within 15 minutes (ethyl or amyl alcohol). 15 grains dissolved in ½ fluid ounce of water, to which are added 10 drops of argentic nitrate solution and 1 drop of ammonia, should not give a mirror or precipitate metallic silver

when warmed (aldehyde). As already stated the liquid is hygroscopic, and therefore control must be kept upon the presence of water by the boiling point (which it lowers), and by agitation of 2 fl. drachms with 10 grains of exsiccated cupric sulphate; no powerful blue colour should be produced.

Medicinal Uses.—In intensity of action amylene hydrate stands between chloral hydrate and paraldehyde. Prof. I. v. Mering first recommended it as a safe hypnotic, specially in cases of nervous sleeplessness, being without action on the respiration or heart. It has been successfully given to children in whooping cough in doses of 3 grs. The adult dose is 45 to 60 grs. Care must be taken to prescribe the remedy with sufficient water to completely dissolve it, thus:

℞	Amylen. hydrat.	100 grs.
	Extr. glycyrrh. liq.	ʒij
	Aqua. dest. ad.	ʒij

M. Half to be taken in the evening before going to rest

This mixture is undoubtedly preferable to the capsules as a means of administration.

The hypnotic was also given in red wine, with raspberry syrup, &c., by Drs. Avellis, Gürtler, Mayer, Rosenbach, Wilde r muth and others, with generally satisfactory results. It was found to be not only hypnotic, but in some cases anodyne also. After the remedy has been given for some time it seems to have the drawback of not being well borne. In therapeutical activity it is unequal to chloral hydrate and to morphia.

According to Dr. P. Næcke, amylene hydrate in two to five tablespoonful doses of a 10 per cent. aqueous solution is often effective in reducing the number of attacks in most forms of

epilepsy. It does not seem, however, advisable to give it to patients who have previously been taking bromide, as in 35 cases of this kind there was an increase of attacks and great restlessness.

ANTHRAROBIN.

$$C_6H_4 \left\{ \begin{matrix} C(OH) \\ CH \end{matrix} \right\} C_6H_2(OH)_2$$

A phenol derivative allied to chrysophanic acid, and described as a leuco-substance.

Preparation.—By the reduction of commercial alizarine in warm ammoniacal solution with zinc dust, and filtration of the resultant solution into water acidulated with excess of hydrochloric acid. The precipitate is washed by decantation until free from acid, collected on clay plates, and dried at 100° C.

Physical and Chemical Properties.—Commercial anthrarobin is a yellowish white powder, practically insoluble in water and dilute acids. Being a phenol derivative, it dissolves readily in the cold in dilute aqueous solutions of the alkalies and alkaline earths, these solutions being brownish-yellow, and greedily absorbing oxygen (by which alizarine is reformed). Anthrarobin is difficultly soluble in chloroform and benzol, but readily in 5 parts of alcohol; also soluble in glycerine.

Twenty-four grains should dissolve in ½ fl. oz. of soda solution to a clear solution, which assumes a violet colour if air is passed through it (1 grain absorbs 120—130 grain measures of oxygen). Should not leave more than 1—2 per cent. of residue when burned on platinum foil.

Medicinal Uses.—Anthrarobin was recommended by G. Behrend in skin diseases generally, where chrysarobin had been successfully used. Professors Liebermann and Pick also recorded its advantages as a non-staining and non-irritant application. Later observers (Drs. Rosenthal and Koebner), on the other hand,

characterised it as practically worthless, and it seems to have gone out of use. Possibly the difference of opinion may have been due to variations in the composition of the article, as commercial alizarine is not a simple body, and, therefore, the product of its reduction would also contain other constituents than that represented by the above formula, and probably in uncertain proportions.

ANTIPYRIN.

(Dimethylphenylpyrazolon; Phenazone).

$$C_6H_5N \begin{cases} CO.CH. \\ NCH_3.\ CCH_3 \end{cases}$$

A synthetical base which forms salts analogous to those of ammonia.

Preparation.—According to Knorr's patent by the interaction of phenylhydrazine and acetylacetic acid whereby phenylhydrazineacetylacetate is formed. By the action of heat this splits up into ethyl alcohol and phenylmethylpyrazolon, and the methylation of the latter in the presence of methyl iodide completes the process, antipyrin hydriodide being actually formed.

By another method, recently patented, it is made by the condensation of a halogen butyrate and phenylhydrazine; the methylphenylpyrazine resulting is converted by a weak oxidising agent into dehydromethylphenylpyrazine, and this by methylation yields dehydrodimethylphenylpyrazine (=Dimethylphenylpyrazolon).

Physical and Chemical Properties.—Antipyrin occurs in odourless and colourless scaly crystals, with a somewhat bitter taste. The melting point of the pure compound is 113° C. (B.P. Add. 110° C.); it is readily soluble in water, rectified spirit and chloroform, but less soluble in ether (about 1 in 50). Ignited with free access of air, it burns away without residue (absence of inorganic contamination).

The absence of free acid is insured by requiring the aqueous

solution to react neutral to test-paper, and of metals, by providing that the passage of sulphuretted hydrogen shall produce no effect. By nitrous acid the solution is turned a deep green colour; this is one of the tests for identity adopted by the B.P. Add. Another given by the same authority involves the production of a yellow colour by the action of nitric acid, which deepens to crimson on warming, while the ferric chloride reaction—production of a deep red colour, nearly discharged by excess of dilute sulphuric acid—is also inserted. This latter test distinguishes antipyrin from other organic substances, which produce various colours with ferric chloride, and differ in the effect of sulphuric acid upon the colour.

Acetanilide has been found admixed with antipyrin. Its detection is very easy, as, though both the compounds have approximate melting points (113° C.), a mixture of equal parts melts at 45° C.

Medicinal Uses.—Antipyrin is given internally as a powerful antipyretic, in doses of 15 to 30 grains, repeated as may be necessary. It is also largely employed as an anti-rheumatic and anti-neuralgic. Other uses of antipyrin are in whooping cough, and as a hæmostatic in hæmorrhoids, epistaxis, &c., in chorea and in asthma bronchiale. In a few cases it had been tried in the treatment of diabetes, with some success. Antipyrin has been recommended as a remedy, or rather, a prophylactic against sea sickness, and in combination with $\frac{1}{8}$ grain cocaine against nausea of all kinds. Externally, its antiseptic properties have sometimes been requisitioned, and it has a limited application by means of the hypodermic needle; local irritation seems to have sometimes followed its use in this way.

Antipyrin has the advantage over most other synthetical antipyretics of being freely soluble in water so that it can be dispensed in solution, or (if prescribed in powder) dissolved in water by the patient before taking.

The remedy is also one of the many drugs much prescribed in the compressed form, introduced into this country by S. M. Burroughs and H. S. Wellcome.

Though a fairly stable body, antipyrin is more or less decomposed or thrown out of solution by a number of other chemical compounds and galenicals—a fact which it is of considerable importance to bear in mind in dealing with mixtures of which it forms an ingredient. From the full list of drugs and preparations found by Messrs. Millard and Stark to be incompatible with the newer substance, the following are taken as more important :—

Acid. hydrocyan. dil.
Acid. tannic.
Butyl-chloral hydras.
Chloral hydras (in strong solution).
Dec. cinchonæ.
Ext. cinchonæ liq.
Ferri sulph.
Ferric salts in solution.
Inf. catechu conc.
Inf. cinch. acid.
Inf. rosæ acid.
Inf. uvæ ursi.
Liq. arsen. et hydrarg. iod.
Nitrites in solution, All acid.
Sodii salicylas (solid).
Tinctures containing tannin or iron.
Tinct. hamamelid.
Tinct. iodi.

Chloral forms, according to Choay and Béhal, several compounds with antipyrin, as mono-, di-chloralantipyrin and an acetyl derivative of mono-chloralantipyrin. One of these bodies has been brought under the notice of the medical profession as *Hypnal*, and credited with useful hypnotic properties. This preparation is readily prepared (Demande) by mixing a solution of 47 grammes (1½ ounces troy) of chloral hydrate in 50 cc. (1¾ fluid ounces) of distilled water, with a solution of 53 grammes (1¾ ounces troy, less 22 grains) of antipyrin in 50 cc. of distilled water, pouring into a separating funnel and drawing off, after an hour, the oily-looking liquid from the supernatant aqueous layer. At the end of 24 hours the separated liquid will have solidified to a mass of

rhombic crystals, and some small rhombs will also have formed in the aqueous liquid. These should be drained and dried on bibulous paper or under a cold dessicator.

The formation of the green colouration produced by nitrites takes place with spirit of nitre, so that the two should not be prescribed together; at the same time, it should be said that *Isonitroso-antipyrin* as the body is termed, has been itself tried in medicine.

The reaction of sodium salicylate and antipyrin does not appear to be the result of a chemical change, but of deliquescence, the sodium salicylate acting as a carrier of moisture to the more soluble antipyrin. A definite salicylate of antipyrin seems, however, to be possible, and under the name

Salipyrin has been brought under medical notice. Prepared by the inter-action of antipyrin and salicylic acid in substance at 100° C., or in solutions, it occurs as a white, coarsely crystalline, odourless powder, with a rough but not unpleasant sweetish taste, readily soluble in alcohol and benzol, difficultly in ether, and scarcely at all in water. From alcohol it crystallises in hexagonal tables. The melting point is 91.5° C. According to Guttmann, twice as much salipyrin must be given as antipyrin to attain the same antipyretic result. Thus, 1½ drachms were given daily in 15-grain doses (increasing to 30 grains) in high continuous fever, while in remittent fever half that quantity was sufficient. In chronic articular rheumatism and rheumatic sciatica, salipyrin was successful; like all other remedies it did not prevent relapse in acute articular rheumatism. The only unpleasant subsidiary symptom observed was a transient papulous eruption (in a single case).

Another salt, *Citrate of antipyrin* has also been put forward and employed, but does not seem to possess any well-marked advantages over the base.

Iodopyrin, or *iodantipyrin*, is said to be a compound in which

one atom of the hydrogen in the phenyl group of antipyrin is replaced by hydrogen. It is described as crystallising in colourless, lustrous, prismatic needles, melting at 160° C., and without taste or marked odour. It is difficultly soluble in cold water and in alcohol, but readily in both liquids hot. Doses of 8 to 24 grains cause a fall of temperature and perspiration ; in these doses no collapse has been seen, and the return rise of temperature is without shivering (Münzer). It is still uncertain whether the compound has any advantages over antipyrin and an alkaline iodide in mixture.

Resopyrin, another antipyrin compound, is described under resorcin.

ARISTOL.

(Dithymoldiiodide.)

$$\left.\begin{matrix} C_3H_7 \\ CH_3 \end{matrix}\right\} C_6H_2(OI)C—C(OI)H_2C_6 \left\{\begin{matrix} C_3H_7 \\ CH_3 \end{matrix}\right.$$

A somewhat unstable amorphous powder, believed to result from the condensation of two molecules of thymol, and the substitution of the hydrogen of the OH group and of one CH group in each by iodine. It contains about 46 per cent. of iodine. It was first introduced under the name *Annidalin* but subsequently rechristened and again brought out.

Preparation.—Aristol may be prepared by the decomposition of a solution of iodine in iodide of potassium by an alcoholic solution of thymol. In order to insure uniformity in the product many precautions have to be taken, as it does not seem to be the product of very well defined chemical action.

Physical and Chemical Properties.—A brownish red, odourless, amorphous powder, insoluble in water and glycerine, slightly soluble in alcohol, and readily in ether ; also taken up by fatty oils when rubbed together with them. Aristol is easily decomposed

by light and heat, and hence all solutions should be made without the aid of the latter, and kept from the action of the former force

Soon after the introduction Langgaard stated that aristol gave up its iodine with great readiness to substances with an affinity for it, and pointed out that thereupon depended certain restrictions in its use.

Recently manufactured specimens of this compound have been found to be less contaminated with free iodine than earlier batches, but it still contains alkaline iodide (Reuter). It may be purified from the latter by solution in cold, glacial, acetic acid, precipitation with water, thorough washing of the precipitate, and drying at 60° C. The pale yellow product dissolves clearly and without residue in ether, and also contains no free iodine.

Medicinal Uses.—Aristol was first used by Eichhoff in various skin diseases in the form of an ointment. He found it superior to iodoform in being odourless, and only second to it in activity where indolent soft ulcers were concerned. So remarkable was the effect in lupus, that Eichhoff believed it to be a specific poison to the *Bacillus tuberculosis*, at the same time as it stimulated the growth of fresh granulations. Dr. Schirren used it in psoriasis with good results, but thought less of its effect on lupus. As a 10 per cent. solution in flexile collodium, Schuster also recommended it in psoriasis, and specially in the ulcerative processes of tertiary syphilis. A considerable number of other medical men in Germany, in Spain and in France spoke in favour of the antiseptic in all cases where iodoform had been previously used, thus in gynæcology, dermatology, diseases of the ear, nose, pharynx, syphilidology, &c.

The most convenient forms of using aristol are as unmixed powder, as ointment with vaselin or lanoline 5—10 per cent., in solution in oil or ether (same strength), and as zinc-starch paste (10 per cent.) In gynæcology suppositories have been ordered containing 8-15 grains of aristol each, with cacao butter. A

useful liniment for certain cases is made by dissolving 5 grs. of aristol in 2 drms. of a mixture of equal parts of ether and alcohol and incorporating with 1 oz. of soft soap.

As already mentioned, under chemical properties, aristol is decomposed by admixture with substances having a strong affinity for iodine, but a zinc-starch paste containing it is said to remain unchanged.

Doubt has recently been thrown upon the efficacy of perfectly pure and, therefore, fairly stable aristol. Probably in the same direction lies the explanation of the unsatisfactory results sometimes obtained, such as those of Professor Neisser, who found the substance quite inactive save in some cases of lupus, where it followed the application of a caustic.

BENZANILIDE.

(Benzoyl-anilide.)

$C_6H_5NH\ COC_6H_5$.

A crystalline compound bearing the same relation to benzoic acid as acetanilide to acetic acid.

Preparation.—By the action of benzoyl chloride or of benzoic anhydride on aniline, the reaction being thus represented :—

$$C_6H_5NH_2 + C_6H_5COCl = HCl + C_6H_5NH\ C_6H_5CO.$$

Physical and Chemical Properties.—Colourless, micaceous, lustrous, scaly crystals, insoluble in water, soluble in alcohol. Melting point 163°C; at a higher temperature distils unchanged.

Medicinal Uses.—First commended by Çahn and Hepp as an antifebrile specially suitable for children ; the dose being 3 to 8 grains, according to age ; and later by Kahn, of Frankfort. It produced exanthema sometimes, and apparently had not sufficiently marked advantages to insure its retention in materia medica ; at any rate nothing had been added to the literature of benzanilide or a considerable time.

BENZOSOL.

(Benzoyl-guaiacol.)

$C_6H_4OCH_3OCOC_6H_5$.

A crystalline compound of guaiacol in which the hydrogen atom of the hydroxyl is replaced by benzoyl.

Preparation.—By formation of a potassium salt from crude guaiacol and purification of the salt by re-crystallisation from alcohol. The pure product is then warmed with the calculated amount of benzoyl-chloride, and the resultant benzosol re-crystallised from alcohol. Also by the interaction of guaiacol with benzoic anhydride.

Physical and Chemical Properties.—A colourless crystalline powder, almost odourless and tasteless. Melting point 50°C. Insoluble in water, readily soluble in hot alcohol, in ether and in chloroform.

Medicinal Uses. — Benzosol was introduced as a comparatively tasteless combination in which guaiacol could be given in large doses, without affecting the digestive apparatus or causing eructations. In the intestinal tract it appears to split up into guaiacol and benzoic acid, and is excreted in these combinations with the urine. By Dr. F. Walzer it was given (in doses of 4 grains, gradually increasing to 12 grains) to 10 patients with good results, weight and appetite increasing and expectoration and cough decreasing.

The compound is made by more than one firm, and there is reason to believe that the products are different. At least, one of them is reported by Professor Sahli to have a different smell and odour to that described above, and this in large doses, 1½ to 2 drachms daily, and with continued use, had no effect at all upon the disease. Sahli concluded that the effect of guaiacol, and creosote were due to local antiseptic action in the stomach, and

hence could not be substituted by benzosol, but evidently the subject is not sufficiently investigated to enable sound judgment to be made.

By Dr. Walzer the compound was given in powder or in pastilles of sugar and chocolate, or with addition of oil or spirit of peppermint.

BETOL.

(Naphtalol; Naphtosalol; Salinaphtol).

$C_6H_4OH\ COOC_{10}H_7$

A crystalline compound with the composition of a β-naphtol salicylate, and closely allied to salol.

Preparation.—By heating together a mixture of β-naphtol-sodium, sodium salicylate and phosphoric chloride; besides betol, sodium meta-phosphate and sodium chloride are formed.

Physical and Chemical Properties.—When pure, betol forms a colourless, odourless and tasteless, lustrous, crystalline powder, melting at 95°C. Insoluble in water or glycerine, soluble with difficulty in alcohol and turpentine, readily so in boiling alcohol (1:3), in ether, benzol, and in warm linseed oil.

Betol is a fairly stable body, unaffected in the cold by alkalies or acids (unless very strong); when heated with these reagents in strong solutions it splits up into salicylic acid and β-naphtol.

Absence of free salicylic acid is proved by pouring a few drops of an alcohol solution into very dilute ferric chloride solution, when no colour should be produced. The compound is distinguished from salol by its much higher melting point (salol = 43°C), and by the production of a pure lemon-yellow coloured solution with pure concentrated sulphuric acid, which a trace of nitric acid changes to olive brownish-green. With salol no such colour results.

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Absence of free salicylic acid is proved by pouring a few drops of an alcohol solution into very dilute ferric chloride solution, when no colour should be produced. The compound is distinguished from salol by its much higher melting point (salol = 43°C), and by the production of a pure lemon-yellow coloured solution with pure concentrated sulphuric acid, which a trace of nitric acid changes to olive brownish-green. With salol no such colour results.

Inorganic impurities, chlorides, phosphates, &c., are detected in the usual manner. Impure preparations are said to assume a blue or reddish tint on keeping.

Medicinal Uses.—At first it was expected that betol would prove equally as valuable as salol, but its higher melting point and chemical stability proved to be disadvantages which restricted its use. At the same time its lower degree of solubility also told against it, and although it was used internally (in vesical catarrh and rheumatism, dose 5—8 grs.) and externally (especially in gonorrhœa) both on the Continent and in England, it seems to have almost entirely fallen out of sight now.

BROMOFORM.

(Tribromomethane.)

$CHBr_3$

An analogue of chloroform, discovered in 1832 by Löwig.

Preparation.—By the action of bromine upon a solution of equal parts of caustic potash and methyl alcohol. The separated bromoform is washed with sodium carbonate solution freed from water with calcium chloride and rectified.

Physical and Chemical Properties.—A clear colourless liquid when pure, with a peculiar but not unpleasant odour and a sweet taste. Specific gravity 2.9, and boiling point 147°-148°C. Bromoform is only very slightly soluble in water, 8 or 10 drops in 6 ounces of water, but readily in alcohol. When evaporated by gas or lamp-light, bromine and a bromine compound ($COBr_2$)—very irritating to the mucous membrane of the throat and conjunctiva—are apparently produced, analogous to the chlorine and phosgene gas formed from chloroform under similar conditions.

Bromoform for medicinal use must be free from acid and colour.

Yellowish specimens are unfit for administration until they have been purified by washing with dilute soda solution, and drying over calcium chloride. Pure bromoform also does not attack the mucous membrane like chloroform. It must be kept out of sunlight.

Medicinal Uses.—The employment of bromoform in medicine was originated in 1889, by Dr. H. Stepp, who announced it to be a remedy for whooping cough in daily doses of 5, 10, 15 to 20 drops, dissolved in 4 ounces of water, with addition of spirit. Thus :—

℞. Bromoformi	.. ..	gtt. x.
Sp. vini rect.	.. ..	♏ 45—60.
Aq. dest.	.. ..	ad ʒ iv.

A little syrup and flavouring might also be added. Stepp afterwards recommended it to be dispensed unmixed, and so many drops ordered to be taken in water or coffee, &c. Drs. Neumann and Löwenthal, though not regarding bromoform as a specific against whooping cough, pronounced it to be equal to any and superior to most other remedies, while having the advantages of a pleasant taste and convenience of administration.

Very recently two cases of poisoning with bromoform from overdoses have been described by independent authors. In both instances the patients—children of 4 and 4½ years—obtained access to the bottle of medicine and drank the whole, amounting in one case to about 10 drops, and in the other to 20 or 30. Deep narcosis supervened, preceded by a short stage of alcoholic intoxication. Injections of ether in one (**Bromethane.**) fresh air with prolonged practice of artificial respiration, the other, were eventually successful, and concentrated sulphuric acid recovery felt quite well. It is evident that, placed in a retort, and carefully restricted, and it would seem added in small portions keeping practice of sending out the unmixed. When the reaction is complete

CHINOLINE.

C_9H_7N

A tertiary amine, first prepared by the distillation of cinchonine and subsequently synthesised by Bayer, Königs and others.

Preparation.—Either by extracting the elements of water from hydrocarbostyril with phosphorus pentachloride or by the action of caustic soda upon the mixture of acrolein, nitrobenzol and aniline, formed when nitrobenzol, aniline, glycerine and sulphuric acid are heated together. The chinoline obtained is purified by fractionation and precipitation from alcoholic solution as sulphate or by ebullition with chromic acid.

Physical and Chemical Properties.—Pure chinoline is a colourless liquid with a pungent characteristic aromatic odour. Specific gravity at 15°C., 1.084; boiling point 237°C. Very slightly soluble in water (though hygroscopic), freely so in alcohol, ether and chloroform.

By the action of light and air chinoline is rapidly turned brown; it is decolorised by shaking with solid potash or soda and slow rectification.

We Chinoline forms by direct addition of acids crystalline salts
Ph which are mostly hygroscopic, and double salts with the metals.
when pure the action of fuming sulphuric acid chinoline is converted
taste. Specinoline sulphonic acid, which, when melted with potash,
form is only very chinoline, C_9H_6NOH.
of water, but reac he compound may be contaminated by water (which
lamp-light, bromine ing point), by homologous compounds (which
irritating to the mucous m or nitrobenzol and hydrocarbons. Aniline,
are apparently produced, a t colour with chlorinated lime solution, and
gas formed from chloroform un carbons separate as oily drops when

Bromoform for medicinal use m s of concentrated sulphuric acid and

Medicinal Uses.—Chinoline has been recommended as an antiseptic, but its employment *per se* in medicine has always been quite insignificant. It is more interesting as the base of other compounds.

Of the salts of chinoline, the tartrate and salicylate were chiefly introduced into commerce, and used both internally (8-15 grs.) and externally. *Chinoline tartrate* occurs in long, white rhombic crystals with a faint odour of bitter almond oil; soluble in 70 to 80 parts of cold, more abundantly in hot water. The *Salicylate* is a white crystalline powder, soluble in water 1-3) and glycerine; very soluble in alcohol, ether, vaseline and atty oils.

Kairin, or ethyl-kairin, $C_9H_{10}(C_2H_5)NO\,HCl$, prepared from chinoline, through α-chinolin sulphonic acid, α-oxy-chinolin, and α-oxychinolintetrahydride, was one of the first substitutes for quinine prepared by synthesis. It was recommended by Filehne as an antifebrile, but its use was attended with considerable risk, and subsequently it was displaced by the antipyretics later discovered and is now no longer manufactured.

The so-called *Kairin M.* was hydrochloride of α-oxychinolinmethyltetrahydride $C_9H_{19}(CH_3)NO\,HCl$, whilst *Kairolin A.*, and *Kairolin M.*, were the acid sulphates of ethyl- chinolintetrahydride and methylchinolintetrahydride respectively.

CHLORALAMIDE.

(Chloralformamide). (Trichloromethane.)

$CCl_3CH.OH.CONH_2$

Preparation.—By the interaction of concentrated sulphuric acid hydrate) and formamide according to the ol, placed in a retort, and ded in small portions keeping

$CCl_3CHO + CHONH_2 = C$ When the reaction is complete

Physical and Chemical Pro

anhydride, and the cresalol is purified by repeated crystallisations from alcohol.

Physical and Chemical Properties.—All three isomeric cresalols are bulky, white crystalline powders, with a saloloid odour. They are insoluble in water, readily soluble in alcohol and in ether, and slightly taken up by oils. Ortho-cresalol melts at 35° C., meto-cresalol at 74° C. and para-cresalol at 39° C.

Medicinal Uses.—The experiments of Bircher showed that meta-cresalol is most suitable for external use as an antiseptic dusting powder, because it has a melting point some distance above the body temperature, and therefore does not "ball." Poisoning symptoms were not noticed with the compound, while it seemed to lessen the secretion of wounds more than iodoform, besides being odourless. Nencki recommends para-cresalol for producing asepsis of the intestinal tract, believing it to be superior to salol for this purpose.

Besides the cresol salicylates there are other similar combinations awaiting the attention of the physiologist and therapeutist, among which are various *Cresol cresotates*, such as *m*-cresol *o*-cresotate (melting point 57° C.), *p*-cresol *p*-cresotate (melting point, 75° C.), and certain *Phenol cresotates*, as phenol *m*-cresotate (melting point 47° C.), and phenol *p*-cresotate (melting point 93° C.)

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of water, but rea
lamp-light, bromine
irritating to the mucous
are apparently produced, a
gas formed from chloroform u
Bromoform for medicinal use

CRESOTIC ACIDS.

(Cresosalicylic Acids; Oxytoluic Acids.)

$C_6H_3CH_3OHCOOH$.

which three are distinguished as ortho-, acids, are homologous with the ortho-

Preparation.—By the interaction of sodium and carbon dioxide and the three isomeric cresols, according to the well-known Kolbe's method of synthesising salicylic acid. They may also be prepared (1) by melting sulphonic acids of the aromatic series $C_nH_{2n-8}O_2$ with caustic alkali; (2) by melting the homologues of phenol with excess of potassium; (3) by the oxidation of their aldehydes, and, (4) by the substitution of an hydroxyl group in the phenoene nucleus of the toluic acids.

Physical and Chemical Properties.—These three cresotic acids crystallise in long white prismatic needles, volatile in steam. They are very difficultly soluble in cold water, somewhat more so in hot, and readily in alcohol, ether, and chloroform. They have different melting points, viz.—ortho, 160° C.; meta, 177° C.; and para, 151° C. Their aqueous solutions are coloured violet by ferric chloride, and in other reactions exhibit a resemblance to the salicylic acids.

Medicinal Uses.—Drs. C. E. Buss (the introducer of salicylic acid into medicine), Koranyi and Gatti used "cresotate of sodium" as an antipyretic so far back as 1876-9. In the latter year it was found that the salt was a mixture of chiefly *p.*-cresotate of sodium with variable quantities of the *o.*- and *m.*-compounds, and for some ten years the investigation was carried no furthor. In 1888 Professor Demme showed that the three acids possessed very different physiological properties, the orth variety being a pronounced heart poison, the meta practi inert, and the para intermediate in action (and less p than salicylic acid). The latter acid therefore has exclusivcly used in medicine.

• ɔbromethane.)

Sodium paracresotate, the most imp a finely crystalline white powder, centrated sulphuric acid repulsive taste; soluble in 24 part ool, placed in a retort, and separation on cooling. It has added in small portions keeping an antipyretic and in the t e. When the reaction is complete

regarded by him as superior to the salicylate of soda in the absence of the secondary disturbing effects on the digestive organs which so often follow the use of the latter. It has also been, and is being used in this country by Professor T. R. Fraser in Edinburgh, and by other well-known authorities, while the researches of Henne (Berne University) have now established beyond doubt the perfect safety of paracresotate of sodium when taken internally, even in very large doses.

The *Cresols* ($C_6H_4CH_3OH$) themselves, or at least the meta and para varieties, have also been used in medicine as more active and less poisonous substitutes for phenol (Fraenkel). Ortho-cresol melts at 31° C., and boils at 185° to 186° C., meta-cresol is a thick liquid, which does not solidify even at -80° C., and boils at 195° to 200° C., and para-cresol forms colourless prisms, melting at 36° C. and boiling at 198° C.

DIURETIN.

(Sodio-Theobromine Salicylate.)

$C_7H_7NaN_4O_2,C_6H_4OHCOONa.$

Synonym.—A definite double compound of sodium theobromine and sodium salicylate.

Preparation.—By the interaction of molecular weights of theobromine and sodium salicylate in aqueous solution, Evidently evaporation to dryness.

Physical and Chemical Properties.—A white powder soluble its weight of water when warmed, the solution cooling. Theoretically, it should contain bromine and 38.1 per cent. of salicylic ted according to the amount of ueous solution is acidified, then

made alkaline with ammonia, and the separated theobromine collected on a filter, washed and dried. By this method a pure compound should yield at least 46.5 per cent. of alkaloid.

Further characteristics of pure diuretin are that it burns away without residue, and dissolves readily and completely in soda solution.

The salicylic acid may be determined by shaking out the acidified filtrate and washings from the theobromine, with ether, separating the extract, evaporating off the solvent and weighing the residue. It should not be more than 38.5 per cent.

Caffeine is detected by dissolving the precipitated alkaloid by addition of potash, shaking out the solution with chloroform, and evaporating off the menstruum; residue amounting to more than ½ per cent. of the alkaloid taken is made up to its actual percentage by the more soluble caffeine.

Medicinal Uses.—Diuretin was first given by Dr. C. Gram, who spoke very highly of its properties as a pure diuretic without effect on the heart. He used it in doses of 15 grains, giving from 45 to 90 grains daily. Dr. v. Schroeder advised that it should be administered in mixture with peppermint water and syrup; and Dr. Koritschoner gave it in 38 cases of severe dropsy with very good results in 23 cases, and satisfactory effect in 10 other patients. The remedy has been also successfully given in England.

ETHYL BROMIDE.

(**Bromethyl**; **Æther bromatus**; **Monobromethane.**)

C_2H_5Br.

Preparation.—Alcohol and pure concentrated sulphuric acid are mixed together, allowed to cool, placed in a retort, and powdered bromide of potassium added in small portions keeping the mixture as cool as possible. When the reaction is complete

distillation is effected at 125° C., on a sand-bath. The distillate is purified by washing with potassium carbonate and water, subsequent removal of water by chloride of calcium, admixture of 10 per cent. by weight of fresh almond or olive oil, and redistillation from a water bath.

Physical and Chemical Properties.—A colourless, limpid, inflammable liquid, with a sweet chloroformic odour and a burning taste. It boils, when pure, between 38° and 39° C.; specific gravity 1.38 to 1.39 at 15° C. Not miscible with water, but freely with alcohol, ether, chloroform and oils. Under the combined action of air and light it decomposes, becoming gradually brown and acid in reaction (free bromine and hydrobromic acid).

These impurities are detected by shaking with an equal volume of water, and testing the latter with blue litmus paper and argentic nitrate, when, if hydrobromic acid be present, the former is reddened and the latter precipitated. Traces of free bromine are evidenced by the violet colour of the globules, which reach the bottom of a potassium iodide solution a little more than an inch deep, when a few drops of ethyl bromide are allowed to slowly fall into it. Shaken with an equal volume of pure concentrated sulphuric acid, no colouration should be produced after 24 hours (ethylene and amyl compounds). Of course preparations with the slightest pungent or unpleasant smell are quite unfit for use in medicine.

Medicinal Uses. — Ethyl bromide has found a place in therapeutical literature by virtue of the rapid and transient anæsthesia which it produces when inhaled. Narcosis is produced in from ½ to 1 minute, and does not last much longer, unless fresh quantities be administered. Consciousness is not altogether lost, but the sensation of pain is absent. The field of usefulness for bromethyl is in minor and dental surgery; it is said to be contra-indicated in cases of alcoholism, and of bronchial, renal, or cardiac disease.

Ethylene bromide has been sometimes confused with and dispensed for ethyl bromide with serious results, as the former is a distinctly poisonous substance. It has however been recently used in doses of 1 or 2 ms. three times a day as an antepileptic.

Ethyl chloride C_2H_5Cl, a colourless liquid with an ethereal odour and boiling at 10° C., has been recommended as a local anæsthetic. The liquid has been introduced into practice (dental surgery, neuralgias) in small tubes with a fused capillary point. The latter is broken off, and then the heat of the hand is sufficient to drive out the contents through the minute orifice in a thin stream, which can be directed to any desired point. The compound is inflammable.

EUPHORINE.

(Phenyl-urethane.)

$NHC_6H_5COOC_2H_5$

A crystalline compound allied both to carbaminic acid and to acetanilide.

Preparation.—By the interaction of aniline and chlorocarbonic ethyl ether.

Physical and Chemical Properties.—A white crystalline powder with a faint aromatic odour, and slight after-taste of cloves. Practically insoluble in water, readily soluble in alcohol or in mixtures of water and alcohol, such as wines. Melting point 51° C.

Medicinal Uses.—Phenyl-urethane was first given as an antipyretic and antirheumatic by Professor Giacosa, of Turin, who stated that in doses of 8 grains it was an energetic and safe antifebrile, also possessing a beneficial effect on the general health. He also found that as an antirheumatic it relieved pain, and reduced the swelling of the joints. Dr. Sansoni also spoke highly of the antithermic effect of euphorine

and the absence of collapse and cyanosis. Against rheumatism he ordered daily doses of 20 to 30 grains, and about the same quantities sufficed to relieve the pain of orchitis, sciatica and tabes dorsalis. Dr. Sansoni used the powdered compound as an application to old ulcers and chronic cases of ophthalmia with very encouraging results, so that he specially urges further trial of the antiseptic properties of phenyl-urethane. Dr. F. Adler, rom an experience of 30 cases, pronounces it to be almost always reliable and rapid in action, and free from unpleasant subsidiary symptoms. The cases included various neuralgias, hemicrania, rheumatic affections, and the remedy was given in doses of 6 grains, three, four and five times a day, according to need; it was prescribed in wafers, dissolved in white wine, or suspended in water.

EXALGIN.

(Methylacetanilide.)

$C_6H_5N(CH_3)CH_3CO.$

A crystalline compound allied to acetanilide, first described by A. W. v. Hofmann in 1874.

Preparation.—By warming together monomethylaniline and acetyl chloride. The reaction when once started takes place violently, and is represented as under:—

$$2C_6H_5NHCH_3 + CH_3COCl = C_6H_5N(CH_3)CH_3CO + C_6H_5NHCH_3\,HCl.$$

The monomethylacetanilide is obtained by dissolving the mass in boiling water and crystallising out. The unchanged methylaniline is recovered by distillation from excess of soda.

Physical and Chemical Properties.—Exalgin occurs in beautiful acicular needles, difficultly soluble in cold water, more

easily so in dilute and concentrated alcohol. It melts at 100° C., and boils between 240°—250° C. without decomposition.

It is converted by soda incompletely, and more readily be concentrated hydrochloric acid, into monomethylaniline. Aniline and other compounds of the base are detected, if present, by the production of a violet colour when solution of chlorinated lime is added to the solution of monomethylaniline in hydrochloric acid after it has been nearly neutralised by ammonia.

Acetanilide and aniline salts are also detected by the odour of isonitril produced when the impure exalgin is heated with alcoholic potash and chloroform. By the provision that the aqueous solution shall not be changed by silver nitrate the absence of hydrochloric acid is ensured.

Exalgin is distinguished from acetanilide, methacetin and phenacetin by treating 2 grains with 20 minims of concentrated hydrochloric acid: insoluble = phenacetin. Acetanilide dissolves, but separates again in crystals. Methacetin also dissolves, but the solution is gradually coloured reddish-brown on the addition of one drop of concentrated nitric acid.

Something has been written as to the possible confusion of exalgin and strychnine, but there seems to be no more danger in this direction with exalgin than with the number of other organic compounds which crystallise in the same form.

Medicinal Uses.—Though exalgin does possess antithermic properties they appear to be exerted only when toxic doses are given (T. R. Fraser). Its chief employment is in the relief of pain of all kinds, whence the name (from ἐξ and ἄλγος pain). The dose used varied between ½ grain and 4 grains, and it is recommended not to exceed 5 grains. In the first few months of the introduction of exalgin into England, there were considerable differences of opinion as to the dose, but the limits cited are now generally adopted. The analgesic is prescribed against neuralgias, sciatica, rheumatism, &c.

Recently it has also been given in chorea, with success, in daily doses of 3 grains (Moncorvo). A good form of administration is the mixture as under:—

℞ Exalgini .. .. 48 grs.
Solve in
Tr. cort. aur. .. .. ʒiss
et adde
Syr. cort. aur. .. .. ʒj.
Aqua .. .. ad ʒvj.
M.f.m.—Each tablespoonful dose contains 4 grains.

GUAIACOL.

(Methylpyrocatechin.)

$C_6H_4OHOCH_3$

A liquid compound constituting from 60 to 90 per cent. of creosote.

Preparation—By fractional distillation of beechwood-tar creosote, the fraction passing over between 200° and 205° C. being collected. This is freed from acid compounds by agitation with ammonia and fractionated again. The lower boiling fraction is dissolved in an equal volume of ether and decomposed with a concentrated alcoholic solution of potash, potassium-guaiacol being formed. This is washed with ether, crystallised from alcohol and the guaiacol set free by dilute sulphuric acid.

Physical and Chemical Properties.—A colourless liquid with a powerful aromatic odour, specific gravity at 15° C. 1.117. Boiling point 200—202° C. Very slightly soluble in water, but readily in alcohol and ether.

The alcoholic solution gives, on the addition of a trace of ferric chloride, a blue colour which turns to emerald green when more ferric chloride is added. This reaction is characteristic.

Guaiacol forms crystalline salts with the metals, an atom of these elements displacing the hydrogen of the hydroxyl group, as potassium guaiacol $C_6H_4OCH_3OK$. The compounds are, however, unstable and decomposed by much water. A stable benzoyl-guaiacol is described under the name *Benzosol.*

So-called commercial guaiacol contains only about 35 per cent. of guaiacol and is unfit for medicinal use. It is distinguished by dissolving in twice its volume of glycerine (specific gravity 1.19), and by giving a liquid compound at normal temperatures with an equal volume of soda (specific gravity 1.30), whereas pure guaiacol solidifies into a white crystalline mass.

Medicinal Uses.—Guaiacol was primarily introduced as a substitute for creosote (of which it is the principal ingredient), which was first used by Professor Sommerbrodt in the treatment of phthisis. According to Guttmann, tubercle bacilli are destroyed by blood which contains $\frac{1}{2}$ per mille of creosote, while even half that proportion arrests their growth. On this statement the intensive creosote treatment of phthisis was based, and for it guaiacol was substituted, as being the principal ingredient; doses of 1 minim are given, gradually increased till at least 15 minims are taken per day. The literature of the subject is fairly extensive, and tends to prove that it is distinctly beneficial in the early stages of the disease.

Guaiacol Salicylate ($C_6H_4OHCO_2C_6H_4OCH_3$) has also been introduced into commerce as a mild guaiacol preparation.

Guaiacol Carboxylate is obtained by saturating sodium-guaiacol with carbon dioxide, heating the mixture in closed vessels to 100° C, and separating the acid from the product by treatment with a mineral acid. The compound is credited with antiseptic and antipyretic properties.

Styracol is described as the cinnamic acid ester of guaiacol, or cinnamyl-guaiacol represented by the formula

$C_6H_5.CH : CH.COOC_6H_4OCH_3$. It is prepared by the interaction of equal molecules of guaiacol and cinnamyl chloride, the mixture being heated for a short time on a water bath, after two hours standing. The resultant mass is treated with boiling alcohol, the solution filtered and allowed to cool; long needles are deposited, which are purified by re-crystallisation. The pure product melts at 130° C. Styracol is said to be a strong antiseptic, useful when administered internally in chronic vesical catarrh, gonorrhœa, and catarrhal affections of the digestive tract. It was also introduced as a substitute for guaiacol in the treatment of phthisis.

HYDRACETIN.

(Pyrodin ; Acetylphenylhydrazine.)

$C_6H_5\,HN\text{-}NHCH_3CO.$

A crystalline compound which may be regarded as hydrazine, (*v.* Hydroxylamine) $H_2N\text{-}NH_2$, in which hydrogen atoms are replaced by the monivalent groups phenyl and acetyl.

Preparation.—By heating together phenylhydrazine and acetic anhydride, dissolving the product in boiling water and crystallising.

$$2C_6H_5N\text{-}NH_2 + (CH_3CO)_2O = 2C_6H_5HN\text{-}NH\ CH_3CO + H_2O$$

Also by the prolonged action of glacial acetic acid on phenylhydrazine distilling off excess of acid and crystallising.

The name "Pyrodin" appeared first in literature under the authority of Dr. Dreschfeld in England at the end of 1888, but a few weeks subsequent to the first paper, the above named author explained that pyrodin was an impure acetylphenylhydrazine.

Physical and Chemical Properties—Colourless hexagonal lustrous prisms, odourless and practically tasteless; melting

point 128°—129° C. Soluble in 50 parts of water at 15° C. and in in 8—10 parts of the same solvent at 100° C.

Boiled with concentrated hydrochloric acid it splits up into acetic acid and hydrochlorate of phenylhydrazine. Like methacetin and phenacetin it forms a colourless solution with sulphuric acid, which is turned red by nitric acid. Added to a solution of silver nitrate lustrous metallic silver is thrown down, and similarly it precipitates gold from auric chloride, flecks of metal appearing on the surface of the liquid.

The absence of acetic acid is shown by the neutrality of solutions. Boiled a few minutes with 30 parts of concentrated hydrochloric acid it dissolves; if chlorinated lime solution is added to the cold liquid diluted with 100 parts of water, a yellow, but no violet, tint is produced (acetanilide).

Medicinal Uses.—Both pyrodin and hydracetin, its principal constituent, were recommended and used as antipyretics, and also applied externally in skin diseases as a substitute for chrysarobin, &c. In neither of these directions, however, has it achieved much success. It is evidently, like phenylhydrazine, a blood poison, and its action is said to be cumulative. It affects the general wellbeing, producing malaise, weakness, and a kind of angina. Cyanosis is frequently reported, and transient albuminaria. Even in the face of the fairly satisfactory results recorded by Guttmann and others, these objections are somewhat serious; further, even those who speak best of it emphasise the importance of very careful dosage, and of watchfulness on the part of the physician, whether it be internally or externally applied. The dose is $\frac{1}{6}$ to 1 grain, not exceeding 2 grains daily, and then not longer than three days consecutively. Externally as a 20 per cent. ointment with lanoline.

The older literature of pyrodin, as it was first of all exclusively termed, must not be referred to as a guide in the posology of

hydracetin, as the former article was an impure aud dilute preparation, which was safely given in doses which would be very dangerous if adopted for the latter.

HYDROXYLAMINE HYDROCHLORIDE.

$NH_2OH\ HCl$.

A crystalline salt of a base analogous to ammonia, and known in the free state only in solution.

Preparation.—By the interaction at o° C. of sodium hydrogen sulphite in concentrated solution and sodium nitrite. The readily soluble sodium salt is by the addition of potassium chloride converted into the difficultly soluble potassium hydroxylamindisulphonate. By the action of heat upon solution of the latter it is split up into hydroxylamine sulphate and potassium sulphate which are separated by fractional crystallisation, and from the former the hydrochloride is obtained by decomposition with barium chloride. The two reactions may be represented as follow:—

$$NaNO_2 + 2NaHSO_3 = HO.\ N(SO_3Na)_2 + NaOH$$
$$2HO\,N(SO_3K)_2 + 4H_2O = (NH_2OH)_2\,H_2SO_4 + 2K_2SO_4 + H_2SO_4.$$

Physical and Chemical Properties.—Colourless hygroscopic crystals similar in form to ammonium chloride. Soluble in an equal weight of water, also in glycerine and in 15 parts of alcohol. The solutions redden blue litmus, but do not affect congo-paper provided hydrochloric acid be absent.

Chemically the compound is distinguished by an enormous reducing power, precipitating metallic gold, silver and mercury from solutions of their salts, and throwing down cuprous oxide from Fehling's solution in the cold. The hydroxylamine itself is oxidised thereby to nitrous or nitric oxide and nitrogen acids.

Iron is detected by potassium ferricyanide or thiocyanide; barium by sulphuric acid; and fixed impurities generally by ignition, when no residue should be left. It is distinguished from sal ammoniac by forming a clear solution with 20 parts of absolute alcohol.

Hydrochloric acid is volumetrically estimated by normal potash, using phenolphthalein as an indicator, and hydroxylamine, by excess of decinormal iodine solution, decomposing the excess with sodium thiosulphate and titrating back with $\frac{n}{10}$ iodine, using starch as an indicator.

$$2NH_2OH\,HCl + 4I = N_2O + 2HCl + 4HI + H_2O.$$

Hydroxylamine hydrochloride must be kept in well closed bottles.

Medicinal Uses.—Binz suggested the use of this compound as a non-staining substitute for the reducing bodies, pyrogallic acid, chrysarobin and antharobin, in the treatment of skin diseases. Subcutaneously it is a powerful poison, and under all conditions antagonistic to vegetable and animal life. As to its value there is no little diversity of opinion. Eichhoff and Fabry found it effective in the treatment of lupus, mycosis tonsurans and sycosis parasitaria, while Groddeck and others not only pronounced it useless but dangerous if absorbed.

Hydrazine or diamine, N_2H_4, is a somewhat allied and similarly reducing body. It is also a general poison to animal and vegetable life; germinating cotyledonous plants and algæ, infusoria, crustaceans, and insect larvae, young snakes and rabbits being alike killed by it according to O. Loew and H. Buchner. Peptone solutions containing 1 per mille of diamine sulphate are no longer able to support bacterial life, and the solutions remain unchanged for weeks. Diamine also kills the germs of mould.

HYPNONE.

(Acetophenone; Methylphenylketone.)

$C_6H_5\,CO\,CH_3$.

A liquid compound long known to the chemist and classified among mixed ketones.

Preparation.—By the dry distillation of calcium acetate and calcium benzoate. The crude product (containing about 6 per cent. of hypnone) is purified (from toluol, diphenyl ketone and cumarin) by repeated fractional distillation, solidified by cold the adhering liquid removed by bibulous paper and again rectified. The reaction by which methylphenylketone is formed is probably

$$\left.\begin{matrix}CH_3COO\\CH_3COO\end{matrix}\right\}Ca + \left.\begin{matrix}C_6H_5COO\\C_6H_5COO\end{matrix}\right\}Ca = 2CaCO_3 + 2\left\{\begin{matrix}CH_3\\C_6H_5\end{matrix}\right\rangle CO.$$

Physical and Chemical Properties.—When pure, hypnone is a colourless oily liquid, with a peculiar odour and a pungent taste. Specific gravity, 1.032; at 14° C. it solidifies, melting again at 20°.5 C. (Staedel and Kleinschmidt). Very little soluble in water, but readily miscible with alcohol, ether and fatty oils.

Chemically, hypnone has all the properties of a true ketone, but does not form a crystalline compound with sodium hydrogen sulphite. Free acids must not be present, therefore it should not alter blue litmus paper, and the absence of benzaldehyde and cumarin is required by providing that one drop of hypnone in 3 drachms of $\frac{n}{1000}$ permanganate must not decolorise the latter within two minutes.

Medicinal Uses.—Dujardin-Beaumetz first recommended methylphenylketone as a hypnotic in 1885. It was said to be superior to chloral and paraldehyde, though as the blood pressure was reduced and the respiration affected by its administration care was enjoined in using it. Drs. Seifert and

Rottenbiller reported upon its employment in 1887, the latter recording its failure in the treatment of psychical diseases, and the former the rapidity with which the patients became habituated to the compound, so that it no longer produced any effect. Since the last mentioned date nothing of importance has been published on the application of hypnone.

Hypnone must be distinguished from *Hypnal* to which reference is made under " Antipyrin."

ICHTHYOL.

(Ammonium Ichthyol Sulphonate.)

$C_{28}H_{36}S_3O_6\ (NH_4)_2$.

The most important of the salts of ichthyolsulphonic acid, prepared from a bituminous mineral of Tyrol, which is rich in fossilised remains of fish and sea animals, whence the name "ichthyol" (ἰχθύς fish).

Preparation.—By dry distillation of the bituminous mineral, there passes over, between 100° C and 225° C a crude volatile oil. This is treated at 100° C with an excess of concentrated sulphuric acid, the resultant ichthyolsulphonic acid precipitated several times by concentrated brine to obtain it free from excess of acid.

Physical and Chemical Properties.—The product of the process outlined above contains a certain proportion of unchanged volatile oil, which gives it a peculiar odour. This oil cannot be removed without bringing about decomposition.

The product of the saturation of the ichthyolsulphonic acid with ammonia is a clear reddish-brown viscid liquid, with a bituminous odour and taste. It is miscible with water (the mixtures being faintly acid); alcohol and ether dissolve it in part; benzin takes up very little. From aqueous solutions hydrochloric acid throws down a dark resinous mass, soluble in ether and in water (but not in dilute acids or solution of sodium

chloride). The action of potash devolopes the odour of ammonia, and the mixture dried and carbonised forms a mass which gives off sulphuretted hydrogen when treated with hydrochloric acid. Dried in a water-bath, ichthyol loses about 45 per cent. of its weight.

Medicinal Properties and Uses.—The application of ichthyol in medicine apparently depends chiefly upon two properties—(1) Its contractile effect upon the vascular system, and (2) its reducing and antiseptic qualities. Upon these properties are based the indications for its use, both externally and internally, in skin diseases, in pain, hyperæmia and inflammation from divers causes, and in numerous affections caused by, or associated with, anomalies of the circulatory system. Its antiseptic power has been recently placed beyond doubt by the work of Dr. J. Fessler, who found that 1 in 4,000 of ichthyol arrested the growth of the bacteria of erysipelas and of pus. Recently, the most prominence has been given by the writings of Freund, Reitmann, Schoenauer, Kötschau and others to the use of ichthyol in the diseases of women, where by virtue of its great power of subduing pain and imflammation it is especially indicated. Attention has also been drawn by Dr. Lehmann to its anodyne properties in the treatment of neuralgias, sciatica and the like.

Externally, ichthyol is used as ointment with lanoline, as liniments, wool, soap, &c. It plays an important part in the modern treatment of skin diseases. In gynæcology a 10 per cent. solution in glycerine is largely employed, and against erysipelas a 25 per cent. collodium (ichthyol and ether of each 5 parts, collodium 10 parts). Internally, the dose is 5 to 20 ms. in mixture or (as sodium salt) in pills.

Other salts of ichthyolsulphonic acid are the ichthyolsulphonates of sodium, lithium, zinc and mercury. They all occur

as brownish, black, tar-like masses, but the first is the only one of any importance. Being solid it is employed when it is desired to give ichthyol in pill form.

Thiol is the name under which a rival to ichthyol has been brought under the notice of the medical profession. It is made according to a patented process) by heating unsaturated hydrocarbons, as found in the so-called "gas-oil," with sulphur until sulphuretted hydrogen ceases to be evolved, and then sulphurating by the action of an equal weight of concentrated sulphuric acid. The product is treated with water and the resulting resinoid mass freed from adherent acid and unchanged mineral oil by kneading with water, neutralising with ammonia, and extracting with solvents. Solid thiol and a concentrated aqueous solution are introduced into commerce.

Thiolum siccum occurs as brownish-black scales, or a dark brown powder with a feeble bituminous odour and bitter astringent taste. The liquid is brownish-red, and neutral. In general physical characters the preparations resemble ichthyol.

Primarily recommended by Reeps and Buzzi for the same purposes as ichthyol with the advantage of having a les pronounced odour and taste. It seems to have been successfully used by Dr. E. Schwimmer and by Möller in veterinary practice, but its literature at present is meagre.

IODOL.

(Tetriodpyrrol).

C_4I_4NH.

A crystalline compound first prepared in 1885 by Ciamician and Silber.

Preparation.—By the interaction during 24 hours of iodine and pyrrol in alcoholic solutions. The mixture is then diluted with water, when the iodol separates in crystalline yellow flocks,

$$C_4H_4NH + 8I = 4HI + C_4I_4NH;$$

or the presence of hydriodic acid may be avoided by using aqueous solutions of pyrrol with soda or potash, and of iodine with potassium or sodium iodide, collecting the precipitate, dissolving in alcohol, decolorising with animal charcoal and reprecipitating. There are also other methods involving the use of metallic oxides for the same purpose.

Physical and Chemical Properties.—Pure iodol is a pale yellow, more or less crystalline, bulky powder, free from odour and taste. It is practically insoluble in water, and slightly soluble in diluted alcohol. Strong alcohol takes up a third of its weight, which is precipitated from solution by water but not by glycerine. Ether dissolves its own weight of iodol, and fatty oils about one-fifteenth.

When heated gradually iodol is unaffected up to 100°—120° C., but between 140° and 150° C. it is decomposed with the evolution of violet iodine vapours; if the heat is maintained it finally burns away without residue.

Metals, if present, are detected by sulphuretted hydrogen, and iodides by argentic nitrate.

Medicinal Uses.—Iodol was introduced as an antiseptic iodine compound, suitable for replacing iodoform, and having the advantages of being free from odour and toxic effects. It can be employed, like iodoform, as a dusting powder, or in alcoholic or ethereal solution, with collodium, in ointment or as gauze. For application to the mucous membrane, a powder consisting of larger crystals is preferable, as not "balling" like the ordinary powder. Iodol is specially recommended in the treatment of tertiary syphilitic lesions, soft ulcers, buboes, &c. It has also

been given internally in doses of 8—15 grains in wafer, as a less energetic substitute for potassium iodide when the treatment is to be long continued.

LANOLINE.

(Adeps Lanæ Hydrosus).

The purified cholesterin fat of sheep's wool containing not more than 30 per cent. of water.

Preparation.—From crude wool fat by emulsification with hydrate or carbonate of the alkalies and "separation" (into a kind of cream and whey) in centrifugal machines. From the "separated" cream the cholesterin fats are set free by addition of solution of calcium chloride, and the impure lanoline thus obtained purified by repeated melting and washing, and finally by extraction with acetone, which does not dissolve the contaminating calcium soap.

Physical and Chemical Properties.—A whitish unctuous substance free from odour. It does not affect moist litmus. Insoluble in water, only partly soluble in alcohol, but readily so in ether, benzene and acetone.

Kneaded with water for some time, lanoline should take up about 100 per cent. of water without slipping smoothly off a spatula ; preparations containing soap exhibit this absence of adhesiveness.

With respect to the proportion of water present, the B.P. Add. requires that 100 grains heated on a water bath till of constant weight shall yield not less than 70 grains. It is further characteristic of a pure preparation that the supernatant layer of fat obtained when the substance is heated with five times its weight of water in a water bath is a clear pale yellow oil.

This supernatant fat (*Adeps Lanæ* B. P. Add.) should be separated from the aqueous liquid and especially examined. According to the B.P. Add. [2nd Ed.] it

should have a melting point between 37°.8 C. and 44°.4 C. [the former figure is certainly too low, as under 40° C. there is hardly any evidence of melting in anhydrous lanoline], and 10 grains should dissolve almost completely in 14 fluid drachms of boiling alcohol, the greater part separating in flocks on cooling. [The intention here is presumably to distinguish lanoline from glycerine fats.] Ignited with free access of air it must also leave but a trace of ash [0.1 per cent. of inorganic salts]; and 50 grains dissolved in 4 fluid drachms of ether, with 2 drops of phenolphthaleïn tincture should not require more than 2 grain measures of volumetric soda solution to produce a permanent red coloration. [This test restricts the allowable amount of free fatty acids present to a trace.] "Heated with solution of soda no ammoniacal odour should be evolved," so that ammonia compounds must not be present.

Of the identity tests for cholesterin that of Salkowsky is adopted, involving the production of a purple red colour when a chloroformic solution is gently poured over sulphuric acid. If the operation be carefully performed the surfaces of contact show a fiery brownish-red zone, which recalls the colour of bromine, while the supernatant layer of chloroform immediately above has a violet tint and the upper portions remain colourless.

Liebermann's test, which involves the production of a colour not given by glycerine fats, consists in dissolving about two grains of lanoline in about 1 fluid drachm of acetic anhydride, and dropping concentrated sulphuric acid into the solution; a rose-red colour is produced, which rapidly changes to green or blue.

Another character which distinguishes lanoline from glycerine fats is that it cannot be saponified by the action of aqueous alkalies. The saponification of lanoline—*i.e.*, the separation of the fatty acids from the cholesterin—is only effected by heating the substance with alcoholic potash or by melting with the solid

hydrate. The peculiar stability of lanoline (its non-liability to rancidity) must be ascribed to this firm combination between the cholesterin and the fat acids.

Medicinal Uses.—The resistance of lanoline to rancidity, and its property of absorbing a large quantity of water without losing its ointment-like consistence, have been the factors which have determined its permanent retention in materia medica as an application to the skin, and as a vehicle for the external employment of medicaments of all kinds. Wool fat, as known, was employed centuries ago, before medicine as now understood had come into being. It fell out of use in consequence of the absence of methods of freeing it from irritating impurities. The use of lanoline is indicated in all cases where it is desired to saturate the skin with fat, as for instance in a certain class of skin diseases, or to affect the deeper tissues as in the inunction treatment of syphilis. Experiments on the length of time after which medicaments (*e.g.* iodine preparations) applied with lanoline to the skin can be detected in the urine, have established the unequalled rapidity with which the substance is absorbed. At the same time lanoline, when pure, has no irritant action, and hence can be employed continuously for prolonged periods. Impure preparations containing free fatty acids are not rarely met with, and these are irritating to the skin as the acids are very energetically absorbed.

Other notable properties of the base are the facility with which it adheres to the mucous membrane (owing to the readiness with which it absorbs water), and its power of arresting the growth of bacteria ; the substance itself is always free from germs.

Quite recently Unna has recommended lanoline for the preparation of creams with solutions of aluminium acetate. hydrogen peroxide, calcium chloride, sulphurous acid and other chemicals soluble in water, and indicated for certain skin diseases. From 20 to 40 parts of the solutions were immediate

parts of a mixture of lanoline (2 parts) and vaseline (1 part). It also has a large field of application in the preparation of medicinal soaps.

For the pharmacist, the great importance of lanoline is found in its adaptability as an ointment base for all kinds of substances. The sole practical objection to the use of the preparation in this way is its stickiness, and this is readily overcome by mixing it, as the writer has previously recommended, with liquid paraffin and ceresin, or with one-third of its weight of vaseline. This diluted lanoline, or unguentum lanolini, as it was named by the deviser, meets all the requirements of a good ointment base, and its value is confirmed by the reports of eminent medical men, such as Dr. Paschkis, of Vienna, who characterises it as the most suitable form in which lanoline can be prescribed.

Unguentum lanolini has not the sometimes unpleasant adhesiveness of the unmixed lanoline, while it has all the useful therapeutical properties of the latter. Any application in solid or liquid form can be readily mixed with it, and the ointment so made will keep good and free from rancidity for an indefinite length of time. Another purely pharmaceutical use of lanoline is as a pill excipient for permanganate of potassium and some other refractory substances.

As a cosmetic, lanoline plays an important part, each of its distinctive properties being of special significance in this application. Cold creams, pomades, milks, emulsions, soaps, &c., are made with it.

METHACETIN.

(Para-acetanisidin; Paraoxymethylacetanilide.)

$C_6H_4.OCH_3.NHCH_3CO.$

A crystalline compound differing from acetanilide in the substitution of a hydrogen atom by the oxymethyl group—OCH_3.

Preparation.—Nitro-phenol is first prepared by the action of melted phenol upon nitric acid (specific gravity 1.34), separation, washing and steam distillation of the oily liquid formed. Orthonitrophenol passes over, and pure paranitrophenol is obtained from the residue by recrystallisation from hot concentrated hydrochloric acid. By the action of soda lye, sodium paranitrophenol is formed, and this, by heating with methyl chloride, yields nitranisol. The reduction of nitranisol to anisidin, and the action of glacial acetic acid upon the latter complete the process, the compound being purified by repeated crystallisation from boiling water. The principal reactions may be represented as under:—

$$\underset{\text{Phenol}}{C_6H_5HO} + HNO_3 = H_2O + \underset{o\text{- and }p\text{-Nitrophenol.}}{C_6H_4OH\ NO_2}$$

$$C_6H_4ONaNO_2 + CH_3Cl = NaCl + \underset{\text{Nitranisol.}}{C_6H_4OCH_3\ NO_2}$$

$$C_6H_4OCH_3NO_2 + 6H = 2H_2O + \underset{\text{Anisidin.}}{C_6H_4OCH_3\ NH_2}$$

$$C_6H_4OCH_3\ NH_2 + CH_3COOH = H_2O + \underset{p\text{-Acetanisidin.}}{C_6H_4OCH_3\ NH\ CH_3CO}$$

Physical and Chemical Properties.—Lustrous scaly crystals free from colour and odour which melt at 127° C., and at higher temperatures distil unchanged. Scarcely soluble in water at 15° C. (1:530), readily so in the same solvent at 100° C. (1:12); the solutions should be neutral. Also abundantly taken up by alcohol, acetone, chloroform, glycerine and fatty oils, especially if warmed; less so by benzole, and only very slightly by carbon bisulphide, benzin, ether and essential oils.

The absence of sulphates, chlorides and iodides is ensured by the usual tests, and inorganic impurities generally by ignition on platinum foil. The compound should form a colourless solution with concentrated sulphuric or hydrochloric acid (carbohydrates darken). With concentrated nitric acid it gives an immediate orange colour, and on cooling a crystalline yellow nitro-product

separates. The distinction of methacetin from antifebrin, phenacetin and exalgin is detailed under the properties of the last-named body, and in the monograph on antifebrin.

Like acetanilide (*q. v.*) methacetin gives the indophenol reaction. When boiled with an insufficiency of water to form a solution methacetin forms an oily liquid, which on cooling solidifies. Phenacetin similarly treated does not melt.

Medicinal Uses.—Methacetin was recommended by Mahnert in 1888 as an antipyretic for children and enfeebled persons, in doses of two to three grains. Profuse perspiration was mentioned as a secondary effect, and in one case, at least, collapse and fall of the temperature to 25° C. (77° F.) was observed. Seidler, Heinz, Pescarolo and others also employed the compound in doses of 5 to 10 grains (average 7 grains) as an antipyretic, and against rheumatism with some success; the first named regarded the substance as particularly worthy of further trial against acute articular rheumatism. Five grains of methacetin are said to be equal to 8 grains of phenacetin or 15 of antipyrin in antifebrile effect.

METHYLAL.

(Methylendimethylether.)

$CH_2(OCH_3)_2$

Preparation.—By the interaction of methyl-alcohol, manganese dioxide and sulphuric acid, distillation of the product and purification by repeated fractional distillation and removal of water by potash. The reactions consist first in the oxidation of the methyl-alcohol to formaldehyde and the reaction of this with undecomposed methyl alcohol, thus:—

$$CH_2O + 2CH_3OH = H_2O + CH_2(OCH_3)_2$$

Physical Properties.—A limpid, colourless liquid, with a

penetrating ethereal odour, of specific gravity 0.855 and boiling point 42° C. Soluble in water (1:3), in alcohol, ether and in fatty and ethereal oils. Like chloroform it is not easily inflamed. It is not altered by alkalies, but is decomposed by concentrated sulphuric acid. The solutions must be neutral. Aldehyde and methyl alcohol are detected, if present, by the decoloration effected, when one drop of volumetric potassium permanganate solution is added to a solution of five drops in three drachms of water, with 10 drops of dilute sulphuric acid.

Medicinal Uses.—Methylal was primarily recommended as a hypnotic, in doses of about 30 to 60 minims in mixture, while also it was employed as an anæsthetic, and externally in the form of ointments and liniments against pain. According to some authors it is an excellent antidote to strychnine.

METHYL CHLORIDE.

(**Chlormethyl**; **Monochlormethane**).

CH_3Cl.

A gaseous compound first prepared by Berthelot.

Preparation.—By the interaction of molecular proportions of methyl alcohol and hydrochloric acid, with or without the addition of chloride of zinc. The gas produced is washed by leading it through water, sulphuric acid, soda solution, then sulphuric acid again, and finally compressing it in metallic cylinders under a pressure of 3—7 atmospheres.

Physical and Chemical Properties.—A colourless gas with an ethereal odour; it burns with a greenish flame though it is not highly inflammable. Soluble in one-fourth its volume of water, much more so in ethyl or methyl alcohol, and freely in ether and chloroform. Under a pressure of five atmospheres at normal temperature, or under normal pressure at -25° C., it is a liquid with a specific gravity of 0.9915 (at -23.7° C.), and boiling

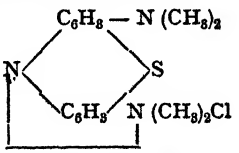
point of -21° C. This liquid should be neutral to test paper and unaffected by silver nitrate or potassium iodide and starch paste.

Medicinal Uses.—So great is the amount of heat absorbed by liquefied chlormethane in reassuming the gaseous condition that it is used to produce local anæsthesia. A stream of the liquid is played upon a tampon of wool and silk placed over the surface to be anæsthetised; the liquefied gas at first saturates the tampon, and then rapidly evaporating therefrom absorbs the heat from the adjacent parts of the body and leaves them bloodless and insensitive. It has been employed against local pain, and in minor surgery. During the past few months Dr. J. Steiner, of Cologne, has spoken well of the treatment in neuralgias, but Dr. B. Schuchardt raises a warning voice to the effect that unless great care be taken tumours, erysipelas, pigmentation of the skin, or even gangrene may occur.

Richardson's compound-liquid is chloroform saturated with methyl chloride. It was recommended as a substitute for pure chloroform as an anæsthetic, but does not appear to have any advantages over the latter.

METHYLENE BLUE.

(Tetramethylthionine chloride.)



A diphenyl amine compound also classed as an "aniline colour."

Physical and Chemical Properties.—Small indigo coloured

scaly crystals with a bronze-like tinge, and dark green in transverse fracture. Slightly soluble in water, forming a deep blue solution which is changed by sulphuric acid to bright green, and from which strong potash solution throws down a dark violet precipitate.

Medicinal uses.—Methylene blue has been given internally in doses of about 3 grains in capsules or pills against rheumatism of the joints and muscles. It appears to have a special affinity or the nerve substance, imparting a blue colour to it, and apparently producing chemical changes in its composition. The urine is also coloured blue within half an hour of the dose. No direct influence seems to be produced upon swelling or exudation, and no ill effects are recorded.

The *Pyoctanins*, blue and yellow, are two other aniline dyes introduced into medicine as antiseptics; the former is said to be "methyl violet" (a mixture of tetra-, penta-, and hexa-methylpararosaniline), and the latter "auramine," an imido-compound of tetramethyldiamidobenzophone, represented by the formula, $2[(CH_3)_2.N.C_6H_4]C:NH$. Solutions of the blue compound ($\frac{1}{3}$-4:10,000) were recommended in general surgery, and of the yellow for ophthalmic practice. Dusting powders, ointments, and dressings were also introduced into commerce. Early in the history of these compounds there appeared a number of reports of which some recorded the non-success of the antiseptics and others warned against irritation and eczema, which might be caused around the points of application. Dr. Petersen more recently found the antiseptics equal to iodoform, and having the advantage of odourlessness. In his hands pyoctanin was very effective in soft and gummatous ulcers, and never gave rise to bad after-effects or toxic symptoms. Dr. Wanscher again spoke very warmly of blue pyoctanin (1 per cent.) in the treatment of blennorrhœa, and of various eye troubles. He also used it in

operating upon the eye with very encouraging results; its power of diminishing irritation is specially pointed out. It further proved effective against suppuration in the nasal passages (Cholewa) and has been recommended in the therapy and surgery of other cavities of the body. Professor v. Mosetig has treated malignant sarcoma, epithelioma and the like with injections of methyl-violet, and believes that complete cure by this method is not impossible.

Apyonin (from α privative and πυον pus) has been newly put forward as a rival to pyoctanin in ophthalmic practice. It is a yellow crystalline powder, little soluble in water, hot or cold, still less so in ether, but abundantly in alcohol. When carefully heated it sublimes, and at higher temperatures burns away without residue. The concentrated aqueous solution is neutral; its colour is altered by neither hydrochloric acid nor nascent oxygen. Potash produces a white precipitate, soluble in alcohol. It has been affirmed to be identical with yellow pyoctanin.

METHYLENE CHLORIDE.

(Dichlormethane.)

CH_2Cl_2

Preparation.—By the action of chlorine on marsh gas, on monochlormethane or on diiodmethane. Also more practically by the reduction of chloroform (in alcoholic solution) by zinc and hydrochloric acid, the product being mixed with water, the specifically heavier liquid separated and purified by successive treatment with soda solution, sulphuric acid, water, chloride of calcium and fractional distillation.

Physical and Chemical Properties.—A colourless liquid resembling chloroform in odour and solubility—specific gravity, 1.354 at 15° C., boiling point, 41°—42° C. Not readily inflammable though the vapours burn with a green-edged flame.

Chloroform, if present, raises the specific gravity. Ethyl or methyl alcohol added as well as chloroform to prevent detection by the gravity are separated by shaking with water, and the dried and redistilled methylene chloride examined again. The separated washing water should give no turbidity with silver nitrate (chlorinated decomposition products) nor blue colour with zinc iodide and starch (chlorine); it should also be neutral to test paper (hydrochloric acid).

Medicinal Uses.—Containing less chlorine than chloroform, methylene chloride was believed by Eichholz and Geuther to be less dangerous, and in 1887 they warmly recommended its use as an anæsthetic. Other physiologists, however, recorded the production of clonic spasms and other nerve disturbances when the compound was used with animals.

It is necessary to clearly distinguish between the definite chemical compound described above and the so-called "English" methylene chloride, or "méthylène" or "Richardson's compound" (*v.* note to methyl chloride).

NAPHTOL.

(Iso or β-Naphtol.)

$C_{10}H_7OH$

A crystalline compound resulting from the substitution of a hydrogen atom in the double ringed naphtalene $C_{10}H_8$ by a hydroxyl group.

Preparation.—By the action of fuming sulphuric acid on naphtalene for several hours at 200° C. The β-naphtalin sulphonate which is chiefly produced is dissolved in water, neutralised with chalk, the calcium salt crystallised out (the α-

salt in more soluble), dissolved in water, converted into sodium salt and the latter decomposed by melted soda as shown under :—

$$\underset{\text{Sodium naphtalinsulphonate}}{C_{10}H_7SO_3Na} + NaOH = Na_2SO_3 + \underset{\text{Naphtol.}}{C_{10}H_7OH}$$

The product is purified by pressure, distillation and recrystallisation from hot water, or from petroleum ether (from which it separates in scales).

Physical and Chemical Properties.—Colourless, lustrous, scaly crystals (or a white crystaline powder), with a faint phenoloid odour, and a transient burning taste; it melts at 123° C., and boils at 286° C. Soluble in alcohol, ether, benzol, chloroform, oils and alkaline liquids. Scarcely soluble in cold, fairly so in hot water (nearly six grains in ʒj.) forming a liquid which, on the addition of ammonia or soda, exhibits a bluish-violet fluorescence, and on the addition of chlorine water a white turbidity changed by ammonia to a clear green, and later, to brown solution. With ferric chloride the hot aqueous solution gives a green tint (violet if α-naphtol be present), but it is unaffected by ferrous sulphate or lead acetate. In the presence of boric acid a solution of the strength of 1 grain in 2 ounces of lukewarm water may be made (Anotta), which acts more energetically as an antiseptic than either boric acid or naphtol alone.

Inorganic impurities are detected by combustion on platinum foil, and α-naphtol by ferric chloride (*v. supra*). Impure specimens are said to be distinguished by darkening when exposed to light. (*cf.* Betol.)

Medicinal Uses. — As an antiseptic naphtol was first introduced into dermatology in 1881 by Kaposi. The literature of the action of the compound since then is not very extensive. Lesser and Neisser recorded symptoms of poisoning which Shoemaker attributed to impurities in the β-naphtol used—a

conclusion largely confirmed in 1888 by an exhaustive pharmacological examination of β-napthol carried out by Willing. Naphtol has been used against skin diseases, organic and parasitic, in ointment form (3-10 per cent.), and in alcoholic solution (2-10 per cent.) In 1 per mille solution it has been highly spoken of as a preservative for anatomical preparations; its powerful bactericidal properties were established by the experiments of Bouchard.

It has been recently observed by a French pharmacist that α naphtol and salol, when rubbed together, form a liquid so that they should not be prescribed in combination. β-naphtol, on the other hand, does not exhibit the phenomenon. The reaction may possibly prove useful in distinguishing the two varieties of naphtol.

Camphorated β-naphtol is a syrupy liquid used with grea success, according to Fernet in the antiseptic treatment of boils, coryza, angina diphtheritica, and tuberculosis. Against the latter it was given by injection in doses of 2 grains mixed with oil. Reboul cured 21 out of 27 cases of tuberculous glands by emptying any abscess formed, and injecting 7—8 drops o camphorated naphtol, repeated every two days. Similar results are recorded by Nelaton.

Hydronaphtol is an American product, described as a derivative of β-naphtol, obtained by reduction, and put forward as an antiseptic and disinfectant free from the toxic action o the parent compound. As to the actual nature of the substance, quite variant opinions have been expressed, and it seems to be still open to doubt. Dr. M. Dockrell used it against tinea onsurans in the form of plaster, a chief indication being to prevent the access of air (oxygen). The affected area was shaved, washed with hydronaphtol soap, and hot water, covered with over-lapping strips of 10 per cent. hydro-

naphtol plaster, and the outside margin of the latter painted over with melted hydronaphtol jelly. At the end of four days the plaster is removed and put on fresh. Two repetitions were sufficient to cure. Mr. K. M. Clarke used it successfully in the treatment of enteric fever and diarrhœa in doses of two or three grains in capsule, or suspended in milk every two hours. In typhoid, 3 or even 4 grains were given to begin with every two hours. As it sometimes interfered with digestion, it has been suggested that it might be given in pills coated with keratin. Dr. Bryce has recently recommended the external use of one part of hydronaphtol dissolved in 10 parts of rectified spirit, to which sufficient glycerine is added to make a 1 per cent. solution. In this form the antiseptic properties of the body were well marked.

α *Oxynaphtoic Acid* ($C_{10}H_6$ OH COOH) is another derivative of naphtol almost insoluble in water, but taken up abundantly by alcohol, ether, benzol, alkalies, and alkaline carbonates. Ellenberger and Hofmeister established the antibacterial properties of the compound, and further, it has been employed as an antiparasitic, against scabies, in the form of a 5 per cent. ointment or as a collodium containing two grains to the ounce.

The hydrocarbon *Naphtalene* $C_{10}H_8$ was also introduced into medicine as an antiseptic and disinfectant both internally, in doses of 2-15 grains, and externally, and also as a safe anthelmintic for children in two grain doses. The observations of Pavas, Dor, Hess, Magnus, and Kolinski among others, led, however, to the conclusion that naphtalene is unsuitable for use in medicine. It acts injuriously upon the optic nerves and the retina, and upon the kidneys, and certainly can only be employed with the greatest care and watchfulness.

It is interesting that a small quantity of camphor, mixed with naphtalene, is said to largely cover the repulsive odour of the latter without affecting its value as a preventive of moth.

preparation, is ensured by the statement that neither chloride of barium nor nitrate of silver must produce a precipitate.

It may be pointed out that even pure paraldehyde may be cooled considerably below 10° C. without solidifying unless it be stirred while the temperature is falling. Specimens containing alcohol or aldehyde may remain liquid at -5° C. From a cold saturated aqueous solution containing 11¾ per cent. of paraldehyde about half of the dissolved compound separates at 100° C. Amyl or valer-aldehyde are detected by the odour of the residue left from evaporation of 2 or 3 drachms on the water-bath.

As paraldehyde is readily converted into acetic acid by oxidation, and even by the action of atmospheric oxygen, it will not often or long be absolutely neutral. It has been, therefore, provided by the P.G. Ed. III. that 1ccm. with an equal volume of acid-free alcohol should not react acid after the addition of 1 drop of normal potash solution.

Medicinal Uses.—Paraldehyde was introduced into materia medica about 1883 as a hypnotic, and made a reputation sufficiently widespread to lead to its adoption into the British and German Pharmacopœias. Physiologically it seems to affect the respiratory centres, but not the heart; its action is antagonised by strychnine. It has also a marked diuretic effect. The sleep produced is characterised as quiet and refreshing, and the remedy said to be valuable in mental and nervous insomnia. The average dose is between 30 and 60 ms., but this limit may be much exceeded.

The pungent taste of the compound may be disguised by prescribing with tincture of orange or some other bitter tincture; it can also be taken in some spirit. Paraldehyde has been used hypodermically (30—60 ms.), but this mode of administration has not found much favour as the hypnotic is rapidly absorbed from the stomach.

By the action of polymerising agents upon aldehyde at a temperature below 0°C *Metaldehyde* ($[C_2H_4O]n$) is formed. It is a white crystalline body insoluble in water, but freely taken up by hot alcohol and ether. When heated it sublimes without melting, between 112°—115° C being at the same time partially decomposed. Metaldehyde has been credited with hypnotic properties.

PHENACETIN.

(Phenacetinum; Acetphenetidin.)

$C_6H_4OC_2H_5NHCH_3CO.$

A crystalline compound closely allied in chemical constitution to acetanilide and methacetin.

Preparation.—Sodium para-nitrophenol (*v.* Preparation of Methacetin) is converted by the action of ethyl iodide into *p*.-nitrophenetol, the latter reduced to *p*.-amidophenetol (*p*.-phenetidin), which by prolonged boiling with glacial acetic acid yields phenacetin. The equation are (*v.* also Methacetin):—

$$\underset{\text{Sodium } p\text{.-nitrophenol}}{C_6H_4ONa\ NO_2} + C_2H_5I = NaI + \underset{p\text{.-Nitrophenetol}}{C_6H_4OC_2H_5\ NO_2}$$

$$C_6H_4OC_2H_5\ NO_2 + 6H = 2H_2O + \underset{p\text{.-Phenetidin.}}{C_6H_4OC_2H_5\ NH_2}$$

$$C_6H_4OC_2H_5\ NH_2 + CH_3COOH = H_2O + \underset{\text{Phenacetin.}}{C_6H_4OC_2H_5\ NH\ CH_3CO.}$$

Physical and Chemical Properties.—The B.P. Addendum describes phenacetin as occurring in colourless, tasteless, inodorous, glistening, scaly crystals, melting at 275° F. (135° C.) sparingly soluble in cold, more freely in boiling-water (1:70, P.G.) and in about 16 fluid parts of rectified spirit.

Phenacetin is officially identified by the production of a deep red colour when chromic acid is added to a cooled and filtered solution of 1 grain in 20 minims of hydrochloric acid diluted with

ten times its volume of water (Ritsert). Its freedom from acetanilide is ensured by the iso-nitrile test, and by providing that a cold saturated aqueous solution shall not become turbid on addition of bromine water. Lastly, sulphuric acid must dissolve it without colour, and heated with free access of air "it burns leaving no residue."

The method of distinguishing phenacetin from similarly constituted bodies is described under exalgin, acetanilide, and methacetin (*q.v.*) Like the two latter, acet-*p*.-phenetidin gives the indophenol reaction. For the detection of 2 or more per cent. on acetanilide in phenacetin, Schroeder recommended boiling 8 grains with about 15 minims of water, cooling, filtering, boiling the filtrate with nitrous acid (or a mixture of potassium nitrite and dilute nitric acid), adding a few drops of Plugge's reagent (a solution of mercurous nitrate containing nitrous acid), and boiling again. In the presence of two or more per cent. of acetanilide the liquid assumes a red colour, due to the production of an azo dye.

When 40 grains of chloral hydrate are melted in a water bath, 8 grains of phenacetin added, and the whole shaken together, solution occurs which in the presence of only traces of para-phenetidin is coloured immediately violet, reddish or bluish in tint, according to the proportion of the impurity present. (Reuter.)

Further phenacetin, free from phenetidin, which, under the same conditions, remains colourless, even when warmed, for at least five minutes, gives a pink-coloured solution after prolonged digestion (identity). A less delicate test is a dilute aqueous iodine solution (1 : 20,000); 8 grains of phenacetin are shaken with 1½ drachms of this solution, and the liquid filtered; a pure compound yields a colourless filtrate (a pink tint = para-phenetidin). Goldmann uses a solution of 8 grains of phenacetin in ½ drachm of spirit; to this the 1½ drachms of iodine solution is added, and the liquid, with the separated

phenacetin, boiled till solution is effected, which is pink if traces of *p*.-phenetidin be present.

Medicinal Uses.—Phenacetin was recommended for therapeutical application as an antifebrile by Kast and Hinsberg in 1887, and its literature, both medical and chemical, is already copious and of wide range. Its reputation as a reliable and safe antipyretic, anti-neuralgic, &c., rests upon the testimony of a host of observers. In relative freedom from collapse (with fall of body-temperature below the normal) and other subsidiary ill effects, the action of phenacetin seems to be equalled by that of few other antipyretics, if any. The only unpleasant symptom which follows its administration appears to be copious perspiration; where fever is complicated by unrest, sleeplessness, &c., phenacetin is reported to reduce the high temperature and produce quiet sleep, not succeeded by headache. The remedy was used with great success during an epidemic of typhus abdominalis in South-East Russia, and in combination with antipyrin in the treatment of the epidemic influenza of Europe in 1889-90. Phenacetin has proved very valuable in neuralgias, in acute articular rheumatism, and in gonorrhoic inflammation of the joints. The antipyretic dose is 8 to 12 grains hourly or every two hours, as may be necessary As an antineuralgic and against rheumatism 15 grains is given for a dose, repeated in some cases till 1½ drachms is taken during the day. It has been beneficially prescribed in 2-grain doses with 12 grains of caffeine citrate against migraine. It is best prescribed and dispensed in powders or readily disintegraing tablets, owing to its slight solubility.

PHENOCOLL HYDROCHLORIDE.

$$C_6H_4\begin{cases} OC_2H_5 \\ NHCO.CH_2NH_2HCl. \end{cases}$$

One of the latest additions to the numerous class of

antipyretics, distinguished by its comparatively free solubility ; is chemically closely related to phenacetin.

Preparation.—By the interaction of phenetidin (para-amidophenetol) and glycocoll or amidoacetic acid. The reaction may be expressed by the following equation :—

$$\underset{\text{Phenetidin.}}{C_6H_4\begin{matrix}OC_2H_5\\NH_2\end{matrix}} + \underset{\text{Glycocoll.}}{HOOCCH_2NH_2} = \underset{\text{Phenocoll.}}{C_6H_4\begin{matrix}OC_2H_5\\NH.COCH_2NH_2\end{matrix}} + H_2O$$

The possibility of forming salts is due to the presence of the amide group.

Physical and Chemical Properties.—Phenocoll hydrochloride occurs in the form of a white micro-crystalline powder, soluble, at 17° C., in about 16 parts of water, and forming a neutral solution. From hot water it crystallises in cubes similarly to antipyrin, from alcohol, in which it is only freely soluble when heated, in needles. Ammonia, the fixed alkalies and their carbonates, throw down the pure base, from a solution of the hydrochloride, in the form of white matted needles, with one molecule of water of crystallisation.

The anhydrous base melts at 100.5° C., but the compound with water at 95° C. Phenocoll is very difficultly soluble in cold, but readily in hot water; it is freely taken up by alcohol, but very little by ether, benzol and chloroform. Dilute solution of the alkalies and their carbonates, and dilute acids, even though boiling, do not readily decompose the base; after prolonged treatment in this way, it partially splits up into phenetidin and glycocoll.

Medicinal Uses.—Professor Kobert primarily established the fact that phenocoll hydrochloride is non-poisonous to animals, and particularly that it does not injuriously affect the blood. In this respect it is therefore superior to phenacetin, of which it may be regarded as a derivative. Experiments were then made on

febrile patients, which indicated that the remedy in doses of 8 grains was a reliable antipyretic, not followed by collapse or cyanosis. Perspiration was not stronger than after larger doses of antipyrin. According to von Mering, 8 grains reduced the febrile temperature as much as 12 to 16 grains of antipyrin. The compound has been also used as a nervine and anti-neuralgic. Phenocoll hydrochloride is preferably given in powder form (wafer &c.), 1¼ drachms divided over 24 hours; in this way complete reduction of fever can be sometimes effected (Hertel). In severe acute articular rheumatism with some fever, the remedy has exerted a beneficial action upon the swollen joints when all other medicaments have failed (Hertel). Phenocoll hydrochloride is rapidly excreted with the urine, which assumes a brownish colour, deepening on exposure to air and giving a still darker cloudy tint with ferric chloride; 12 hours after the administration of the remedy is suspended the iron reaction is no longer obtainable.

PIPERAZINE.

(Piperazidine; Ethylenimine; Diethylendiamine; Dispermine.)

$C_4H_{10}N_2$.

A synthetical compound primarily intended to replace spermine, but found to be a different body in both chemical and physiological characters.

Preparation.—According to a patented process of considerable complexity, probably from hydrochlorate of ethylenediamine.

Physical and Chemical Properties.—Piperazine occurs in well-defined, colourless, acicular crystals readily soluble in water.

According to the manufacturers, the compound brought

together in cold, aqueous solution, with uric acid, dissolves 12 times as much, as carbonate of lithium under the same conditions, and the piperazine urate formed is seven times more soluble in water at 17° C. than urate of lithium. One part of the latter requires 368 parts of water for solution, while one part of piperazine urate is taken up by 50 parts of water. Even when an excess of the acid is present only the readily soluble neutral salt is formed.

Piperazine may be detected in the urine by boiling (to free from any albumen present), acidifying with hydrochloric acid, evaporating to a small bulk and filtering. After addition of concentrated soda solution the liquid is distilled, the distillate acidified, evaporated, filtered and tested by alkaloidal reagents. The double salt of piperazine, with potassium-bismuth iodide, is insoluble in hydrochloric acid, and crystallises in microscopic quadratic tables or pointed needles of red colour; the picrate also forms peculiar yellow microscopic needles, insoluble in hydrochloric acid. The presence of substances like creatin, and sarcosin, which also form precipitates with picric acid, is excluded by the distillation.

Medicinal Uses.—The first to investigate the physiological action of piperazine appears to have been Bock, who examined it in the Pharmacological Institute of Berlin, and reported that he did not observe any stimulant action. Consideration of the behaviour of the base with uric acid referred to above* led to the investigation of its effect upon the urinary organs. Dr. Vogt, of Paris, in conjunction with the chemists Vigier and Gautrelot, believed he had established the fact that the amount of urea in the urine increased during the administration of piperazine,

* It is noteworthy that, according to Professor R. Kobert, *Cadaverine*, $C_5H_{14}N_2$—a ptomaine with some chemical relationship to piperazine—possesses the same property of forming a relatively readily soluble urate.

while the uric acid decreased in quantity. This conclusion has not been confirmed by later observers (Ebstein and Sprague). The compound has also been tried by several authors in mental diseases, with results sufficiently striking to encourage further trials (Umpfenbach, Peretti, Schultze). One investigator records tonic and stimulant effects, and another believes that it may prove to be a valuable diuretic. Its use in a case of lead paralysis was followed by very remarkable results, but at present its value in such cases does not seem to have been fully investigated. The dose of piperazine or the hydrochloride is, subcutaneously, 5 grains *pro die*, and, per os, up to 8 grain several times a day.

PYRIDINE.

C_5H_5N.

A liquid body formerly regarded as constitutionally analogous to chinolin, but recently stated to exhibit differences in behaviour so important that the nitrogen atom is believed to occupy a different position in the molecule of the two compounds.

Preparation.—From bone-oil, by treatment with sulphuric acid, separation of the sulphonic compounds and decomposition with soda. The mixture of bases set free (pyridine, anilines, &c.) is carefully fractionated, the distillate treated with acid oxidising agents (which attack only the aniline bases) neutralised with soda and fractionated again. Small quantities of very pure pyridine are obtained by distilling calcium nicotate with lime, thus:—

$$(C_5H_4NCOO)_2Ca + Ca(OH)_2 = 2CaCO_3 + 2C_5H_5N.$$

Physical and Chemical Properties.—Pure pyridine is a colourless liquid with a peculiar empyreumatic odour and a pungent taste; specific gravity (at 0° C.) 0.9858; boiling point 117° C. Miscible with water in all proportions, and considerably hygroscopic. Pyridine forms salts with acids by direct addition,

like the alkaloids, of many of which, as known, it is regarded as the parent substance. It is distinguished from aniline bases in its power of resisting the action of oxidising agents.

Pyridine should not be altered by exposure to light; it should not contain ammonia (as evidenced by the addition of phenolphthalein to the 10 per cent. aqueous solution), and two drachms of the same aqueous solution to which three drops of volumetric permanganate solution have been added should maintain the red colour for at least an hour (absence of readily oxidizable compounds).

Medicinal Uses.—Pyridine bases are well-known to occur in tobacco-smoke, which have frequently proved beneficial in asthma; Germain Sée therefore proposes the use of pyridine for the relief of asthmatic troubles. From 1 to 1½ drachms are poured on a plate and placed in the room with the patients. In a temperature of 68° F. to 77° F. the above-named quantity is evaporated in about an hour. It is said that after a few minutes of exposure to the pyridine atmosphere the remedy can be detected in the urine. The treatment was well-spoken of by Dr. Kelemen among others, but does not seem to have maintained its ground. Mixed with a little oil of peppermint it has been employed in the topical treatment of diphtheria with some success, and in aqueous solution (1:300) 3 or 4 injections have been recently said to be sufficient to cure gonorrhœa. (Rademacher).

RESORCIN.

(Metadioxybenzole.)

$C_6H_4(OH_2)$.

A compound primarily prepared in 1864 by Barth and Hlasiwetz from umbelliferous resins by fusing with potash.

Preparation.—By converting benzole into benzole disulphonic acid, neutralisation with milk of lime, decomposition with soda,

filtration (to remove the chalk formed), and evaporation to dryness. The product (sodium *m.*-benzoledisulphonate) is fused with caustic soda for eight or nine hours, the mixture allowed to cool, dissolved in boiling water, hydrochloric acid added, the boiling continued till all the sulphurous anhydride has escaped. On cooling the mass is filtered, the filtrate extracted with ether, the latter evaporated off, and the residue heated to 275° C (to remove the last traces of ether and water). The commercial product thus obtained is purified by distillation. The reaction between the sodium *m.*-benzoledisulphonate and sodium hydrate may be represented as follows:—

$$C_6H_4(SO_3Na)_2 + 2\,NaHO = 2\,SO_3Na_2 + C_6H_4(OH)_2$$

Physical and Chemical Properties.—Colourless, or faintly yellowish tabular or columnar crystals, with a scarcely perceptible urinous odour and an unpleasant sweetish pungent taste; when pure and anhydrous it melts at 118° C (100° C to 1:1° C. P.G.) and boils at 276° C. It is readily and abundantly soluble in water (1:1 P.G.), alcohol (2:1 P.G.), and in ether, but scarcely at all so in cold benzol, chloroform and carbon bisulphide.

Heating to the melting point for a few minutes with an equal weight of phthalic anhydride and added to water, the "fluorescein" formed gives the latter an intense yellowish-green fluorescence. 1 grain warmed with 2 grains of tartaric acid and 10 drops of sulphuric acid forms a dark carmine-red liquid.

Inorganic impurities are detected by combustion on platinum foil; phenoloid bodies or acids by the odour and reaction with litmus paper; and empyreumatic impurities by solution in 10 times the weight in water (to which they communicate a yellow tint). Imperfectly refined products are detected by their low melting point; they can be purified by treatment with animal charcoal and crystallisation.

Medicinal Uses.—Closely resembling phenol in its properties, hough less toxic, resorcin has been used externally in substance

or in concentrated solution to effect painless cautery, especially in diphtheria (Andeer), also in the form of ointment (5 to 10 or even to 25 per cent.) against skin diseases, and specially against painful ulcers of the feet (Thoer), and in 1 or 2 per cent. solution for urethral affections. Resorcin wool and gauze have been used in the treatment of wounds. Weak solutions (1 to 3 %) have the property of hardening the skin, while stronger ones (10 to 50 per cent.) macerate and destroy it; upon these observations its use against skin diseases is based.

Internally, it was first used as an antifermentative and against gastric catarrh. Recently it has also been recommended in daily doses of 8 to 45 grains against nausea and vomiting (Andeer), and against asthma (15 grains in water).

Resorcin has given very striking results in the treatment of whooping cough (Moncorvo, Arntzenius, Barlow, Gulas, and others). It is painted on the throat in 1 per cent. aqueous solution.

The remedy is mostly dispensed in aqueous solution, as indicated, against diphtheria. Andeer and others used a 10 per cent. glycerine solution, and gave tablespoonful doses of a mixture of 1 drachm of resorcin in 6 ounces of syrupus terebinthinæ. Injections and sprays were also employed.

Resopyrin is the name of a compound of resorcin and antipyrin obtained by the interaction of molecular proportions in solution; an abundant white precipitate is formed with some included oily drops. On violent agitation the oily mass increases and then suddenly solidifies to a hard white opaque body, resopyrin. From alcoholic solutions it can be obtained in fine rhombic, odourless crystals, insoluble in water, but taken up by ether (1 : 100), by chloroform (1 : 30) and by alcohol (1 : 5); solution in the latter menstruum is not precipitated by water. It differs chemically from resorcin by not giving a precipitate with lead subacetate nor

a blue colour with ferric chloride. When gradually heated it separates into two layers, an oily and an aqueous. The physiological and therapeutical action of this body are still undetermined.

Thioresorcin, $C_6H_4(OS)_2$, is a yellowish-grey tasteless powder, insoluble in water, and only sparingly taken up by alcohol and ether. It was used by Dr. Guttmann as an iodoform substitute for ulcers of the leg. Its application appears to be sometimes followed by unpleasant symptoms (Amon), though these may be traceable to admixture of resorcin.

Fluorescein, or resorcin-phthalein, $C_{20}H_{12}O_5$, occurs as dark-brown crystals, which form with ammonia a red solution, exhibiting a beautiful green fluorescence. Recommended by Dr. Straub for the diagnosis of corneal lesions, and detection of minute foreign bodies imbedded in that tissue. When an aqueous solution is dropped upon the cornea, those parts, however small, which are deprived of their epithelium are coloured green, while foreign bodies are surrounded by a green ring. Dr. Randolph employs a solution of 10 grains to the ounce with 15 grains of sodium bicarbonate.

Hydroquinone, or paradioxybenzol, isomeric with resorcin, is prepared from aniline by oxidation with chromic acid mixture, and reduction of the quinone ($C_6H_4O_2$) formed, by sulphurous acid. It forms long colourless dimorphous crystals, melting at 169° C. difficultly soluble in cold water, readily so in hot water, in alcoho and in ether.

The compound has been employed as an antifermentative and antiseptic. In 1883 it acquired some reputation as an antipyretic (Silvestrini, Picchini, Traversa), the reduction of temperature taking place 30 to 40 minutes after the dose, 6 to 9 grains. Fresh solutions are free from caustic properties, and hence have been used subcutaneously. The internal use of hydroquinone in typhoid has been suggested.

SACCHARIN.

(Benzoyl-sulphonic imide; Gluside; Glucusimide.)

$$C_6H_4 \begin{Bmatrix} CO \\ SO_2 \end{Bmatrix} NH$$

A derivative of the aromatic series distinguished by its powerfully sweet taste.

Preparation.—According to the patent specifications, by conversion of toluol into a sulphonic-acid compound, and of this into a sodium salt. By the action of phosphorus pentachloride the sodium salt is decomposed and a mixture of ortho and para toluol sulphochloride formed; the former isomeride is freed from the latter by cooling (when the para modification crystallises out), and by the action of ammonia converted into orthotoluolsulphamide. The next step is oxidation of the sulphamide into orthosulphaminbenzoic acid, which splits up into water and orthosulphaminbenzoic anhydride or benzoyl-sulphonic imide. The principle reactions are represented as under :—

1) $C_6H_4\begin{matrix}CH_3\\SO_3H\end{matrix} + PCl_5 = POCl_3 + HCl + C_6H_4\begin{matrix}CH_3\\SO_2Cl\end{matrix}$

Toluolsulphonic acid. Toluolsulphochloride

$$C_6H_4\begin{matrix}CH_3\\SO_2Cl\end{matrix} + NH_3 = HCl + C_6H_4\begin{matrix}CH_3\\SO_2NH_2\end{matrix}$$

o.-Toluolsulphamide.

$$C_6H_4\begin{matrix}CH_3\\SO_2NH_2\end{matrix} + 3O = H_2O + C_6H_4\begin{matrix}COOH\\SO_2NH_2\end{matrix}$$

o.-Sulphaminbenzoic acid.

$$C_6H_4\begin{matrix}COOH\\SO_2NH_2\end{matrix} = H_2O + C_6H_4\begin{matrix}CO\\SO_2\end{matrix}NH$$

Saccharin.

Physical and Chemical Properties.—A white, uncertainly-crystalline powder, with an intensely sweet taste and a faint amygdaloid odour. Slightly soluble in cold water (1:400 at 15° C), forming a feebly acid liquid; more soluble in alcohol (1:30) or glycerin; freely so in dilute ammonia, or in solution of sodium bicarbonate (evolving CO_2). According to the British Pharmacopœia Addendum, 1890, 100 parts of gluside mixed with water, warmed, neutralised with bicarbonate of soda, and evaporated to dryness yield 113 parts of soluble gluside or saccharin. Probably in dissolving in water the acid is reformed.

As evidence of identity, the hepar reaction is officially adopted, and the absence of carbohydrates is ensured by providing that neither gluside nor soluble gluside shall be blackened when warmed with strong sulphuric acid.

Further proofs of purity are the absence of residue when heated on platinum foil, of a brown colour when heated with potash lye (grape sugar), and of a red precipitate when warmed with Fehling's solution (natural sugars). Salicylic or benzoic acid if present are detected by the violet colour produced on addition of ferric chloride to the ethereal filtrate, mixed with ten times its volume of water. Mannite is detected by the azure blue colour produced when a solution of soluble saccharin so contaminated is exactly precipitated by cupric sulphate, filtered, sodium lye added and boiled.

According to Dr. Dohome and others, commercial saccharin may contain as little as 40 per cent. of orthobenzoyl-sulphonic imide, the rest being chiefly the isomeric (and non- or less-sweet) para-compound. He states that the substance may be readily tested by treating with ether, which dissolves out the benzoyl sulphonic imide and leaves undissolved all foreign matter.

For the detection and estimation of saccharin in food stuffs of all kinds, and especially in cane sugar, various processes have been suggested. According to Reischauer, 4 ounces of

the suspected material (when this is cane sugar) are treated for a few hours with 6 to 10 oz. of ether and filtered. If a portion of the sugar exhibits an alkaline reaction, instead of the solid substance, a concentrated aqueous solution feebly acidified with phosphoric acid should be shaken out with ether; in both cases the ether takes up the greater part of the saccharin contained in the sugar, which is left as a residue on evaporation and can be recognised by the taste or in the following manner: The residue is melted gradually and carefully (otherwise violent explosion occurs) in a platinum capsule with a mixture of carbonate of soda and nitrate of potassium (6:1) and finally incinerated. The residue, dissolved in water, is tested for sulphates, and the amount of sulphate of barium formed, multiplied by 0.785, gives the weight of saccharin extracted; other compounds of sulphur possibly occurring in sugar are not taken up by the ether.

For the detection of saccharin in urine, C. Schmitt recommends that the liquid should be first tested for salicylic acid. If this be absent, 4 ozs. of the strongly acidified liquid are shaken out three times with a mixture of equal parts of ether and petroleum ether, the extract mixed with soda solution and evaporated to dryness. The residue is heated for half-an-hour in a silver or porcelain capsule to 250° C, the mass dissolved in water acidified with sulphuric acid and shaken out with ether. The ethereal extract on evaporation of the solvent gives the ordinary reactions of salicylic acid (with ferric chloride for instance), produced in the decomposition of any saccharin present.

Beer is neutralised (about 2 pints being used) with sodium carbonate, evaporated to a syrupy consistence, and mixed by assiduous agitation with three or four times the volume of strong alcohol. After a few hours the mixture is filtered (the residue being washed with alcohol), the filtrate distilled, the residue taken up with water, diluted to about four or five ounces, strongly

acidified with phosphoric acid, and shaken out three times with ether, each agitation being continued at least an hour. The ethereal solution is distilled, the residue neutralised with sodium bicarbonate solution, filtered and evaporated to dryness on a watch glass. The residue is recognised as saccharin either by the taste or by conversion into salicylic acid by heating with pure caustic soda to 250° to 270° C.

If salicylic acid be present in the beer, the ethereal residue, neutralised with soda, must be treated with mercuric nitrate, the precipitate (mercuric saccharinate) collected, washed, and dried by pressure between bibulous paper. It is then mixed. by melting, with excess of resorcin, a few drops of concentrated sulphuric acid are added, and the whole again warmed; the mass assumes various colours, froths and resinifies, while sulphur dioxide is given off. On cooling, the mass dissolved in a little water gives with excess of caustic potash a deep brown liquid, with a green fluorescence, which is more pronounced if a few drops be removed and diluted with more water.

Medicinal Uses.—The chief uses of saccharin in medicine are as a sweetening agent for the food of diabetics and as a general flavouring and corrective. For the former purpose its property of passing though the organism unchanged is believed to make it specially applicable. It has also been found beneficial in the treatment of cystitis and urethral inflammation. (Little, Colquhoun.) By far the larger proportion seems to be used in sweetening various foods, confectionery, &c., and a good deal of diversity of opinion has been expressed as to its harmlessness or otherwise when so employed; hence the many processes for its detection in various foods and beverages.

A teaspoonful solution of 5 parts of saccharin in combination with 5 parts of sodium bicarbonate and 5-10 parts of salicylic acid in 24 parts of spirit to a glass of water makes an excellent and agreeable antiseptic mouth wash. Saccharin is conveniently used in the compressed form.

SALOL.

(Phenyl Salicylate.)

$$C_6H_4 \begin{cases} OH \\ COO\,C_6H_5 \end{cases}$$

One of the first organic salicylates introduced into medicine.

Preparation.—Molecular proportions of salicylate of soda and sodium-phenol are caused to react by prolonged heating in the presence of phosphoric oxychloride. The reaction may be expressed as follows :—

$$2\,C_6H_5ONa + 2\,C_6H_4OH\,COO\,Na + P\,O\,Cl_3 = 3\,NaCl + Na\,PO_3 + 2\,C_6H_4\,OHCOOC_6H_5.$$

The product is treated with water, washed till practically free from chloride and phosphate, and finally crystallised from alcohol.

It may also be obtained by leading phosgene gas into a warmed intimate mixture of salicylate of sodium and sodium-phenol. The reaction is quite similar to the above, except that the secondary products are sodium chloride and carbon dioxide.

Physical and Chemical Properties.—A white crystalline powder, or transparent tabular crystals, with a faint aromatic odour, practically tasteless, being insoluble in water. It is taken up by 10 parts of alcohol, or less than its own weight of ether; an alcoholic solution forms with water a kind of emulsion. It is also considerably soluble in copaiba, in sandalwood oil, in turpentine and in fatty or mineral oils. Melting point 42° to 43° C; heated on platinum foil it burns away without residue.

In a solution of ferric chloride, an alcoholic solution of salol produces only a turbidity but no colour; on the other hand, ferric chloride produces in an alcoholic solution of salol the characteristic violet colour of phenol. Bromine water precipitates monobromsalol. The ether is split up by warming with the fixed alkalies into salicylate and alkali-phenol. Treatment

Free acids (salicylic or phosphoric) are detected by blue litmus paper. Free phenol or salicylic acid are evidenced by the behaviour of an alcoholic solution with three times the volume of water, to which previously a drop or two of ferric chloride has been added; a permanent violet colour is produced if these impurities are present.

Medicinal Uses.—Salol was primarily used as an anti-rheumatic, specially in treatment of acute cases. It was also given as an antipyretic, 30 to 45 grains, powder or tablets. In the alkaline liquids of the intestine salol splits up into salicylic acid and phenol compounds, which are excreted with the urine. Upon this property has been based the use of the remedy in acute diarrhœa, dysentery, cholera and other diseases where intestinal antisepsis is indicated (Goelet, Carl Cahall, Moncorvo, Nicholson, Heher, &c.), and also in affections of the bladder and urethra as a substitute for the ordinary mechanical irrigations and injections. Its internal use in the treatment of gonorrhœa has found many supporters, who have placed on record its real value in such cases; copaiba, or sandalwood oil, can be combined with it as adjuvant by simply using it as a solvent for the salol. There are several reports of its more or less successful use against cholera, while it is also being tried in the treatment of leprosy and of yellow fever.

Externally, the compound is used as an antiseptic and deodorant, similarly to iodoform. In ointments and compound powders it has been found the best remedy against impetigo, eczema, and sycosis (Saalfeld), and has also done good service as an insufflation in the treatment of ozæna.

Spirituous solutions (about 5 per cent.) are employed with various flavouring agents for the preparation of mouth-washes and dentifrices, while it is also largely used in the preparation of other soluble antiseptic preparations, *e.g.*, powders and soaps.

used in the comp

SOZOIODOL.

(Diiodparaphenolsulphonic Acid.)

$C_6H_2I_2OHSO_3H$.

A crystalline monobasic acid, introduced in 1887 as an antiseptic; it contains 52.8 per cent. of iodine and 7 per cent. of sulphur.

Preparation.—By the interaction of potassium paraphenolsulphonate, dissolved in dilute hydrochloric acid, and a solution of potassium iodate and iodide, in molecular proportions (or of iodine chloride). Finely-divided iodine first separates, and then again redissolves. After a short time long white needles come out of solution, which are the potassium salt of sozoiodol.

Physical and Chemical Properties.—Sozoiodol crystallises from water in acicular prisms which lose their three molecules of water of crystallisation when exposed over sulphuric acid. It is readily soluble in water, in alcohol, and in glycerine.

The presence of iodide or of chloride is detected by the precipitate formed when argentic nitrate is added to a solution of sozoiodol in nitric acid and of sulphate by the insoluble precipitate formed on the addition of barium chloride. (Barium sozoiodol is soluble in boiling water.)

Medicinal Uses.—Bacteriological experiments prove that 2 per cent. of sozoiodol completely prevents the development of the microbes of pus. According to the statements of physiologists, the iodine of the compound is not separated from it in the organism, so that it is not poisonous. Sozoiodol is said to possess the advantage over other iodine preparations of being absolutely odourless and stable under all normal conditions. It has been used in all cases where iodoform is considered indicated. Either sozoiodol or its salts have been used with a fair amount of success in the treatment of skin

affections, of diseases of the nose and pharynx, of the ear, and of the eye. In syphilis, gonorrhœa, gynæcology, gastric disorders, rheumatisms, &c., it has been also reported to be useful, and without injurious secondary effects. There is some amount of literature further as to its application in dental surgery and in veterinary practice.

Of sozoiodol salts, the most important are the potassium, sodium, mercury, and zinc compounds.

Sozoiodol-potassium.—$C_6H_2I_2(OH)SO_3K$, forms colourless well formed prisms soluble in about 50 parts of water to an acid liquid, which gives a violet-blue with ferric chloride. Fuming nitric acid displaces iodine, picric acid being simultaneously formed. Barium chloride produces a precipitate soluble on boiling.

This salt is less soluble than the sodium compound, and is, therefore, credited with a more lasting action; "it diminishes secretion and is drying." Is specially recommended against eczema.

Sozoiodol-sodium is very similar to the above, but is soluble in about 14 parts of water or of glycerine. The aqueous solution gradually darkens under the influence of light.

Sozoiodol-mercury, $[C_6H_2I_2(OH)SO_3]_2Hg$, is a lemon yellow subtile powder, very readily soluble in sodium chloride solution, but much less so in water (1:500). The 10 per cent. solution is said to be caustic.

Sozoiodol-zinc crystallises in colourless needles with six molecules of water; it is soluble in water (1:20) and in alcohol. Mixed with 10 to 15 parts of French chalk this compound has been used in catarrhal affections of the nose and pharynx.

Other salts which have been prepared and offered for trial in medicine are those of ammonium, lithium, magnesium, lead, silver, and aluminium.

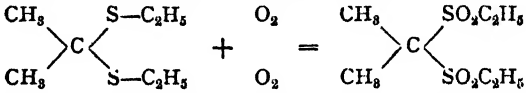
SULPHONAL.

(Diethylsulphon-dimethyl-methane.)

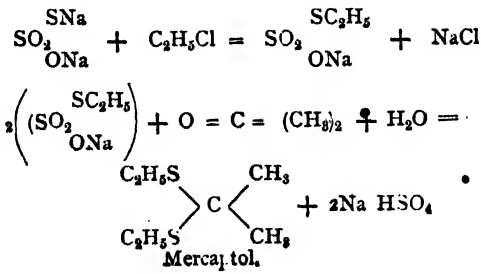
$(CH_3)_2\,C\,(SO_2C_2H_5)_2$.

A synthetical hypnotic which has been admitted to a place in the official materia medica of several European countries.

Preparation. — By the interaction of anhydrous meraptan, and anhydrous acetone in the presence of a stream of dry hydrochloric acid gas. The liquid gradually becomes turbid and separates into two layers, of which the upper is mercaptol (dithioethyldimethylmethane $[CH_3]_2\,C[S\text{-}C_2H_5]_2$), the lower dilute hydrochloric acid (the water is a product of the reaction). The mercaptol is separated, washed, and oxidised by potassium permanganate according to the following equation :—



It is also manufactured by the action of ethyl chloride or bromide on sodium thiosulphate, conversion of the resultant sodium ethyl thiosulphate into ethyl mercaptan and acid sulphate of sodium by the action of water. As this conversion takes place in the presence of alcoholic hydrochloric acid solution and acetone, the ethyl mercaptan is condensed *in statu nascendi* to mercaptol, which is oxidised as above described. The reactions may be represented as under :—



The third stage is the oxidation of mercaptol to sulphonal, already illustrated.

Physical and Chemical Properties.—Colourless, inodorous practically tasteless, prismatic crystals, melting at 125° to 126° C (B. P. Add. 125.5° C). Soluble in 15 parts of boiling water, and in about 450 parts of that solvent cold; also in cold rectified spirit (B. P. Add. in about 50 fluid parts), and freely in boiling alcohol; soluble in ether (1:135 at 15° C).

Sulphonal is a very stable body, being unaffected by concentrated acids, alkalies, or oxidising agents either in the cold or when warm. Chlorine and bromine also are without effect even when warmed. To this stability must be ascribed the lack of a characteristic reaction for the compound.

Officially, sulphonal must burn away without residue when ignited with free access of air. The test of Vulpius, according to which the repulsive odour of mercaptan is evolved when sulphonal is heated with potassium cyanide is recognised in the Pharmacopœia, and it is added further, that "when to the solution of the product in water excess of hydrochloric acid, and a few drops of solution of perchloride of iron are added a reddish colour is developed." This colour is due to the formation of ferric thiocyanide. The same effect may be produced by heating sulphonal with gallic or pyrogallic acid, or with wood charcoal. The reaction is not peculiar to sulphonal, but is produced by the whole classes of sulphones and disulphones and by most mercaptan derivatives.

Further tests of the purity of the compound are that the solutions must be neutral and unaffected by barium or silver nitrate. Two ounces of a hot 2 per cent. solution must not immediately decolorise 6 drops of volumetric potassium permanganate solution.

Medicinal Uses.—In doses of 15 to 45 grains sulphonal is given as a hypnotic specially in the treatment of nervous

sleeplessness. There is, however, a fairly extensive literature of poisoning cases from the administration of the hypnotic, some of which were fatal, and others characterised by eruptions and general severe functional disturbances. Some medical authorities do not regard sulphonal as superior in any respect to previously known hypnotics, while, on the other hand, many, among which are to be numbered several well known English physicians, speak very highly of the reliability and safety of its action. According to W. Svetlin the value of sulphonal as a hypnotic is greatly enhanced by the addition of ½ to 1 grain of codeine to each 15 grains of the remedy.

Owing to the insolubility of the hypnotic it is best taken as powder in wafers or readily disintegrating tablets.

Trional, $C_2H_5CH_3 = C = (SO_2C_2H_5)_2$, differs from sulphonal (as can be seen by comparing the formulas) only in the substitution of an ethyl for a methyl group, so that its systematic name is diethylsulphonmethylethylmethane. It forms lustrous, tabular, bitter crystals, melting at 76°C, requiring 320 parts of cold water for solution, but readily soluble in alcohol and in ether. This compound was expected to be a more powerful hypnotic than sulphonal, from the physiological experiments performed on animals; but Barth and Rumpel found that though evidently indicated in certain nervous diseases where sulphonal did not answer, the dose had to be quite as large (60 grains daily). It seemed to be less liable to produce ill-effects than sulphonal. The same is said to be true of the closely allied

Tetronal, $(C_2H_5)_2 = C = (SO_2C_2H_5)_2$, or diethylsulphondiethylmethane, which occurs in lustrous tabular crystals and plates, melting at 85°C. It is soluble in 450 parts of cold water, readily so in alcohol, and fairly in ether. The taste is camphoraceous and bitter. The name, of course, like "trional," which it physiologically and therapeutically resembles, has reference to the number of ethyl groups present.

THALLINE.

(Tetrahydroparachinanisol).

$C_9H_{10}N\ (OCH_3)$.

A liquid base, first prepared in 1885 by Skraup, who also effected the synthesis of chinoline.

Preparation.—According to the patent specifications from parachinanisol obtained by heating together paraamidoanisol and acrolein (= glycerine + sulphuric acid) in the presence of an oxidising agent (paranitroanisol). By reducing agents parachinanisol takes up four hydrogen atoms forming the base thalline. These two reactions may be represented as follow:—

$$C_6H_4NH_2OCH_3 + O + CH_2CHCHO = C_9H_6N\ (OCH_3) + 2H_2O$$
$$C_9H_6N\ (OCH_3) + 4H = C_9H_{10}N\ (OCH_3)$$

Physical and Chemical Properties.—At ordinary temperatures thalline is an oily liquid, solidifying when cooled to yellowish crystals. It has a strong odour resembling coumarin, and forms well defined salts with acids.

Oxidising agents (the halogens, the nitrates of silver and mercury, chromic acid, ferric chloride, &c.) produce an intense emerald green colour, hence the name (Θάλλος a green twig.)—Ferric chloride produces the colour (which is not affected by addition of a drop or two of pure concentrated sulphuric acid) in very dilute solution (1:100000). Sodium thiosulphate changes the green tint into violet and then into wine-red, oxalic acid at ordinary temperatures into pale yellow, deepening into saffron on heating.

Medicinal Uses.—The base thalline itself is not suitable for use in medicine; and of the possible salts only the sulphate and tartrate have been used.

Thallin sulphate is a yellowish-white crystalline powder with

a coumarin-like odour and a taste described as at once acid, saline, bitter and spicy. Soluble in seven parts of cold or 0.5 part of boiling water; also in alcohol (1:100) difficultly so in chloroform and practically insoluble in ether. The aqueous solutions are acid, and when exposed to light gradually darken; by iodine solution they are precipitated brown, by tannin acid white, and by Nessler's reagent lemon yellow. Like the base itself this salt in 1 per cent. solution is coloured emerald green. When heated over 100° C. thallin sulphate melts, and if the temperature be raised decomposes, burning away (if pure) without residue.

Thallin tartrate occurs as a yellowish-white crystalline powder with an odour reminding of anise and coumarin; soluble in water (1 : 10), slightly so in alcohol, and practically insoluble in ether and in chloroform. In general it behaves like the sulphate, but is distinguished by giving no precipitate with barium nitrate.

Both these salts were at first given internally (doses of 2 to 8 grains) in aqueous solutions as antipyretics, and used externally as antiseptics, specially against gonorrhœa in the form of injections and bougies. Physiological experiments have not encouraged the internal use of thalline compounds; they are poisons for the red blood corpuscles and for the nervous system (Robin, Brouardel, Loye).

As an injection an aqueous solution is recommended containing 4 to 8 grains to the ounce, or a compound solution of thalline sulphate (2 to 5 per cent.) with tannin (0.2 to 0.5 per cent.), and silver nitrate (0.02 to 0.05). Towards the end of the treatment antrophores are employed containing 2 per cent. of thalline or bougies of the same strength made up with cacao-butter.

URETHANE.

(Ethyl-urethane).

$$CO\begin{cases} NH_2 \\ OC_2H_5 \end{cases}$$

One of a series of compounds which may be regarded chemically as esters of carbaminic acid.

Preparation.—By the interaction of nitrate of urea and ethyl alcohol at 120° to 130° C. extraction of the resultant urethane by ether and recrystallisation.

$$\begin{matrix} NH_2HNO_3 \\ CO \\ NH_2 \end{matrix} + HOC_2H_5 = NH_4NO_3 + \begin{matrix} NH_2 \\ CO \\ OC_2H_5 \end{matrix}$$

Physical and Chemical Properties.—Colourless, columnar, or tabular crystals, odourless, and with a nitre-like taste. Readily soluble in water and in most media; the solutions are neutral. Melting point 47° to 50° C.; boils between 170° and 180° C. almost without decomposition, giving off vapours which burn with a blue flame.

Urethane yields carbon dioxide when warmed with sulphuric acid (alcohol and ammonium hydrogen sulphate being also formed), and ammonia (as well as alcohol and potassium carbonate) with caustic potash. If 6 grains are dissolved in a drachm of water, 12 grains of dried sodium carbonate with a few granules of iodine added, and the whole gently warmed, iodoform separates on cooling.

Inorganic impurities are detected by heating on platinum foil; its entire volatility also serves to distinguish it from nitre. Urea is detected if present, by the fact that, in cold aqueous solution, it gives a white precipitate with nitric acid, oxalic acid, or mercuric nitrate.

Medicinal Uses.—Urethane was introduced as a hypnotic in 1885, and recommended by Kobert, Schmiedeberg and others in doses of 15 to 30 grains. Its literature, however, is meagre, and although it was believed to produce a natural sleep, with no ill effects, nothing has been heard of it for some time, and later experimenters report a somewhat large percentage of failures with it. Like some others of the same class of remedies it was credited with antidotal properties for the convulsive poisons (Anrep).

Uralium or *Chloral-urethane.*—Chloral at ordinary temperatures or melted chloral hydrate dissolves urethane; if to such a solution concentrated hydrochloric acid be added it solidifies within 24 hours to a mass insoluble in water. This is then treated with concentrated sulphuric acid and washed with water, by which an oil results which subsequently crystallises.

The product ($CCl_3CH : OH.NHCO_2C_2H_5$) is insoluble in cold and decomposed by boiling water; it is abundantly taken up by alcohol and ether and reprecipitated by water; melting point 103° C. Strongly recommended by Poppi as a hypnotic, more reliable and better borne than chloral. In the hands of Drs. Schmitt and Pariscot, on the contrary, its use was uncertain, and accompanied by unpleasant secondary symptoms.

Somnal.—Under this name a solution of chloral hydrate and urethane in alcohol was introduced as a hypnotic, but, as might have been expected, does not appear to have ever been generally used.

APPENDIX.

The compounds included in this section will be found to fall into two main classes, viz., those which are at least at present of insufficient importance to require detailed description in the body of the work and those which are not purely synthetical remedies.

All those of the former class are however met with and referred to in medical literature, and those of the latter are in many cases of established reputation, so that it has been thought desirable to embody some information respecting their properties and uses in an appendix.

AGARICIN.

This dibasic organic acid $C_{14}H_{27}OH(COOH)_2,H_2O$, homologous to malic acid, was first isolated in the crystalline condition by Fleury in 1870. It is extracted from powdered agaric by alcohol and subsequent purification. Pure agaricin or agaric acid is a white, silky, lustrous, granular, crystalline powder, with a feeble odour and taste, melting at 128°—129° C. Little soluble in cold water; when heated with that liquid it swells up and forms a viscous, frothy solution which deposits on cooling. Soluble in cold (130 parts), and in hot (10 parts) alcohol, more readily in hot acetic acid, less in ether, and very little in chloroform.

Locally, agaricin has powerful irritant effects, and larger doses than 8—15 grains cause vomiting and collapse. $\frac{1}{12}$—$\frac{1}{6}$ grain in pill, with pulv. ipecac. co., is given against the profuse perspiration of phthisical patients, or in order to counteract the sweats

produced by other medicaments. The effect seems to be unaccompanied by functional disturbance, and to last several days.

Anisic Acid.

When anethol (a constituent of anise and fennel oils) is oxidised, a monobasic acid, isomeric with methylsalicylic acid is formed, which has the formula, $C_6H_4(OCH_3)COOH$. Methylparaoxybenzoic acid, as it is systematically called, occurs in colourless prisms, difficultly soluble in cold, but more readily in hot water; soluble in alcohol. It melts at 175° C., and distils without decomposition at 280° C.

This acid is of therapeutical or medicinal interest chiefly as yielding a sodium salt, which was recommended by Curci in 1887 as an antiseptic and antipyretic. It was given in doses of 15 grains, and its action was said to be quite analogous to that of sodium salicylate, though it did not produce the disturbing effects of the latter upon the digestive functions. In spite of this advantage it is certainly very little employed.

Aseptol.

Phenol and concentrated sulphuric acid reacting at a low temperature yield ortho-oxybenzolsulphonic acid, $C_6H_4OH.SO_3H$. A solution made in this way, and diluted till it contains about $33\frac{1}{3}$ per cent. of the above-named sulphonic acid, has been recommended for external use in surgery, &c. It is a syrupy, reddish liquid with a weak phenoloid odour and acid reaction; miscible in all proportions with water, alcohol and glycerine. S.g., 1.155.

Aseptol or *Sozolic acid* was introduced in 1887 as an antiseptic. Drs. Hueppe and Samter obtained evidence of fairly good

bactericidal powers, but the preparation proved very unreliable, and so was practically abandoned.

Aseptol must not be confounded with *Aseptinic acid*, which was an aqueous solution of about 5 per cent. of borax and 3 per cent. of hydrogen peroxide, with sometimes a little salicylic acid; was introduced about 1886 as an antiseptic, but did not succeed in proving its *raison d'être*.

Bromol.

Under this name, *Tribromophenol*, $C_6H_2Br_3OH$, has been recently re-introduced to the medical profession as an antiseptic. When pure it forms white crystals, melting at 95°C., practically insoluble in water, but freely taken up by alcohol, ether, and chloroform; also soluble in glycerine, in fatty and essential oils. The odour is unpleasant, bromine-like, and the taste sweetish-astringent.

Tribromophenol was bacteriologically investigated by Grimm in 1888. "Bromol" is recommended to be used in solution (1 : 30 olive oil) or ointment (1 : 10), as powder or dressing. Against diphtheria a 4 per cent. glycerine solution is to be used. In doses of 1-10th to 1-3rd grain has been given in cholera infantum and typhus abdominalis.

Camphoric Acid.

When camphor is oxidised by nitric acid the compound above-named is formed, having the formula $C_8H_{14}(COOH)_2$. When purified it forms white acicular or scaly crystals, odourless, and with feebly acid taste. Difficultly soluble in cold, but fairly readily soluble in hot water, in alcohol and ether; also taken up by fatty oils. Melting point, 175°—178° C.

Camphoric acid was first applied in 1888 in acute and chronic diseases of the respiratory tract by Dr. Reichert, who used ½—6 per cent. solutions topically in angina, coryza, acute bronchitis, &c. Several authors have cured cystitis by injections of ½—2 per cent. solution, and in doses of 30 grains recommended it against the night sweats of cousumptives. More recently Professor Schultzer and others have also recorded their conviction of the superiority of camphoric acid in such cases to other medicaments.

Chloral Cyanhydrate.

This compound was first prepared by Messrs. Pinner and Bischoff, and ascertained to have the same physiological action as hydrocyanic acid. It is represented by the formula $CCl_3CHOH.CN$, and described as forming colourless prismatic or rhombic crystals readily soluble in water, alcohol, and ether. Aqueous solutions remain unaltered a long time. 6.46 parts by weight correspond to 1 part of prussic acid.

Medicinally, chloral cyanhydrate is used for the preparation of liquids to replace cherry laurel, bitter almond, and other waters containing indefinite proportions of hydrocyanic acid.

Creolin.

A dark brown alkaline liquid containing in solution the higher homologues of phenol. It forms a more or less turbid milky mixture with water possessing the characteristic odour of the preparation.

By virtue of its relative non-poisonousness—nearly half a pint has been taken without fatal issue—and freedom from caustic or even irritating properties, creolin has been very largely adopted in surgical operations as a substitute for carbolic acid. The literature of its use, both in this country and on the Continent

is very voluminous; mainly it shows that creolin is of great value wherever septic odours of any origin have to be overcome, and where a harmless and non-irritating but powerful antiseptic is indicated.

The preparation has been very well spoken of in every department of antiseptic surgery and medicine from gynæcology downwards, while it has also been successfully used internally in gastric fermentation, dysentery, typhoid and the like.

Creolin is used pure, in solution (2 per cent.), and in ointment with lanolin (lano-creolin). A dusting powder (10 per cent.), gauze (10 per cent.), and surgical soap (10 per cent.), are also made. Internally the liquid is given in capsules containing 5 ms. each.

Disinfectol and *Lysol* were the names under which two somewhat similar preparations were put forward as competitors with creolin. Their properties were not essentially different from those of the earlier antiseptic, and they did not exhibit any advantages over it, so that little has been heard of them since their introduction, and their literature is meagre.

Dithiosalicylic Acids.

These compounds, of which some nine isomers seem to be possible, are represented by the formula $HO_2C(OH)C_6H_3S_2C_6H_3(OH)CO_2H$. One of these, hygroscopic and very soluble in alcohol, was discovered by Baum in 1889, and its sodium salt—distinguished as *Sodium dithiosalicylate* "No. II."—was introduced into medicine as an antirheumatic.

In 8 grain doses four or five times daily, it was successful in articular rheumatism, and the *Lithium salt* of the acid proved especially efficacious in the treatment of the same class of disease and gout of long standing (Lindenborn, Frank).

Sodium dithiosalicylate "No. I." has only recently been brought under notice as a powerful antiseptic. In 15 per cent. solution, the most resistant bacilli are destroyed in from two to 15 minutes; in a severe case of ozæna it effected a complete cure in a relatively short time. In 2½—5 per cent. solution, this preparation is reported to have yielded most strikingly beneficial results in the treatment of foot and mouth disease, where its further trial would seem to be very desirable.

EUCALYPTOL.

This oxygenated body, $C_{10}H_{18}O$, was first isolated by E. Jahns from the essential oil of various eucalyptus species. Since then it has been detected in the oils of numerous other plants, and the list now includes 6 species of *Eucalyptus (globulus, amygdalina, dumosa, bayleyana, microcorys* and *oleosa)*, and 15 other plants. When pure it is a colourless liquid with a camphoraceous odour; s.g. 0.930, boiling point 176°—177° C., and crystallising point -1°C. Practically insoluble in water, but miscible with alcohol, ether, chloroform, and fatty oils. Eucalyptol is optically inactive.

Externally the body is used as a stimulant in rheumatism and neuralgias, and, further, in the antiseptic treatment of atonic ulcers, gangrene, &c. Internally it has done good service in chronic bronchitis, pulmonary gangrene, asthma, catarrhal affections of the urinary tract, and the like. Dose, five drops daily in gelatine capsules or in emulsion.

Eucalyptoresorcin.—In contact with excess of resorcin eucalyptol combines in the cold to form a hard pulverulent mass, while on heating a very compact substance results which gradually becomes amorphous and very hard. The new compound, freed from excess of resorcin by solution in chloroform and recrystallisation, forms matted crystals, insoluble in water,

but very soluble in alcohol and ether. Little or no light has at present been thrown upon the composition or properties of this body.

Mercury Compounds.

It would be well to point out that the literature of all these compounds is very meagre; the greater number were introduced for hypodermic injection, as anti-syphilitics, but no one of them seem to have as yet displaced at all generally the emulsions of calomel, yellow oxide, and mercurial ointment.

Mercuric and zinc cyanide.—This preparation, a white powder, entirely insoluble in water, was recently recommended by Sir J. Lister as an antiseptic, non-irritating dressing. It consisted of a certain proportion of mercuric cyanide (not exceeding 36 per cent.), the particles of which were "occluded" from the action of water by the insoluble zinc cyanide (Dunstan). It does not seem to have given in other hands such satisfactory results as were recorded by the eminent surgeon named.

Mercuric benzoate $(C_6H_5COO)_2Hg,H_2O$.—Small crystals free from colour, taste, and odour, sparingly soluble in cold, more readily in hot water and in alcohol. In solution in brine, or suspended in liquid paraffin, was used by Stukowenkow subcutaneously against syphilis, but no further reports appeared upon its value.

Mercuric carbolate or **phenylate** $(C_6H_5O)_2Hg$.—Occurs as colourless needles, practically insoluble in water and cold alcohol, but taken up by hot alcohol (1 : 20), by ether, or a mixture of alcohol and ether, and by glacial acetic acid. Used against syphilis by Schadek in doses of $\frac{1}{3}$—$\frac{1}{2}$ grain (children $\frac{1}{15}$—$\frac{1}{12}$ grain) twice or three times a day.

A basic salt $C_6H_5O(HO)Hg$, not always of constant composition, and occurring as a yellowish white to orange powder, was used by Gamberini.

Mercuric imido - succinate $[C_2H_4(CO)_2N]_2Hg$. — First described in 1852 by Dessaignes, and recommended by v. Mering and Vollert in 1888 as an antisyphilitic. It forms a white lustrous crystalline powder, which gives a clear solution with 25 parts of water, or 300 parts of alcohol. Subcutaneously injected in doses of $\frac{1}{3}$ grain.

Mercuric naphtolate.—A lemon-yellow powder, odourless, insoluble in water; contains 30.8 per cent. of mercury. The dose for internal administration is 1 grain. Naphtolacetate of mercury (similar in constitution to thymolacetate, *q.v.*) is a white crystalline substance. These compounds were tried by Jaddasohn and Zeissing, but found to produce more violent pain than the thymolacetate or salicylate of mercury.

Mercuric oxycyanide.—$Hg_2O(CN)_2$ has newly been spoken highly of as an antiseptic by Boer, according to whom it is superior to sublimate as a germicide while it is neutral, does not coagulate albumen, is less caustic, and does not attack instruments so powerfully.

Mercuric peptonate.—A yellowish liquid, with a saline, feebly metallic taste, and slight acid reaction. Was introduced as a mild and efficient mercurial for hypodermic injection, not causing pain, or producing abscesses. The usual dose was given as 1 ccm., said to correspond to $\frac{1}{6}$ grain of mercuric chloride. A modification of this prepararion has been quite recently brought under medical notice. It is termed

Glutine-peptone sublimate, and described as a double compound of glutine peptone hydrochloride (made by the action of hydrochloric acid on gelatine) with sublimate, containing 25 per cent. of the latter. It forms a white, lustrous powder, hygroscopic, but very stable ; is almost solely offered in the form of a 1 per cent. solution. The dose used by Dr. Hüfler was a

Pravaz' syringeful of solution, which corresponded to about grain of mercuric chloride. The injections were described as accompanied by little pain, and no severe local symptoms, while rapid and efficient in action upon the disease.

Mercuric salicylate $C_6H_4OCO_2Hg$.—A fine, white, neutral powder, free from odour or taste, forming soluble double salts, with the halogen chlorides, bromides, or iodides. It was first recommended in 1887 by Silva-Araujo, and later by Szadek, as a mild but energetic mercurial for internal and external use. Internally the dose was $\frac{1}{60}$—$\frac{1}{8}$ grain, chiefly in pill form; externally it was prescribed in 0.4 per mille solution as an injection in gonorrhœa, and suspended in mucilage for intra-muscular injection. Has perhaps been more widely used than any other of the newer compounds of mercury.

Mercuric tannate.—Somewhat dull brownish-green scales, free from odour and taste; yields tannin to water or alcohol, but is not *per se* soluble in those liquids. Was recommended as an antisyphilitic by Lustgarten, its beneficial action being ascribed to its decomposition by the alkaline fluids of the intestine, metallic mercury being set free. Dose 1 to 2 grains, half to one hour after food.

Mercuric thymolate $(C_{10}H_{13}O)Hg\text{-}HgNO_3$.—When pure this compound, first recommended in England, is said to be perfectly colourless and free from odour, though on exposure it gradually becomes reddish and acquires a faint thymoloid odour. The so-called thymolacetate of mercury has the formula $(C_{10}H_{13}O)Hg\text{-}HgC_2H_3O_2$. Both these compounds (as also a "thymolsulphate") were examined by Kobert and shown to be suitable for therapeutical use against syphilis; chiefly the thymolacetate was employed, in doses of $\frac{1}{12}$ to $\frac{1}{6}$ grain internally as pill, or for intra-muscular injection suspended in paraffin. Pain and infiltration were rare.

MYRTOL.

This is the fraction of the oil of *Myrtus communis*, boiling between 160° and 180° C. It is a clear liquid, of not unpleasant odour, which was recommended (Eichhorst) in doses of 5 ms. twice a day as a reliable and prompt remedy against putrid processes of the respiratory tract. According to E. Jahns, myrtol is a mixture of dextro-pinene and eucalyptol, and would be advisedly replaced by the latter.

SALICYLATES.

Bismuth salicylate $Bi(C_7H_5O_3)_3Bi_2O_3$ is of somewhat uncertain composition, dependent upon the length of time it is subjected to washing with water. Contains about 76 per cent. of bismuth oxide and 23 per cent. of salicylic acid, and is prepared, among several possible ways, by precipitating bismuth nitrate with dilute sodium salicylate solution made feebly alkaline with soda. The precipitate is washed by decantation till the washings no longer give a violet reaction with ferric chloride.

The product so obtained is an amorphous, yellowish-white powder, entirely insoluble in water ; neither alcohol, ether, nor chloroform extracts salicylic acid from it.

Estimation of oxide by gentle incineration must yield at least 60 per cent. Nitric acid is detected if present by the brown ring (which is formed when a mixture of the preparation and an equal weight of sodium salicylate with 10 times the weight of water is floated on concentrated sulphuric acid) and arsenic by Fleitmann's test.

The importance of the tests for free salicylic acid and for the nitric radical is recognised when it is said that various brands of so-called bismuth salicylate have proved on examination to be mere mixtures of salicylic acid and subnitrate of bismuth, mixed

in such proportions that on incineration the amount of oxide left should correspond to that of the pure compound. Other preparations, doubtless made by precipitation, have also been frequently found to contain considerable quantities of free salicylic acid. Such mixtures, or carelessly prepared compounds, irritate the digestive tract when given internally.

Externally, the basic salicylate of bismuth has been employed in medicine as an iodoform substitute in the treatment of wounds, ulcers &c. Internally, it has made a reputation in chronic diseases of the digestive organs and intestines. It is reported to have proved useful in diarrhœas, and in preventing fermentation in the intestines after operation. In doses of 10 to 15 grains two or three times a day as powder it does not seem to cause functional disturbances even when given for a prolonged period.

Lithium salicylate $LiC_7H_5O_3,\frac{1}{2}H_2O$.—A white crystalline powder, soluble in nearly its own weight of water; also abundantly taken up by alcohol. According to Vulpian this salt will usefully supplement the action of sodium salicylate as it removes the last traces of fever in acute articular rheumatism, which often obstinately resist the administration of the sodium combination. Against chronic rheumatism and rheumatic affections of the tendons it is superior to the latter. The average daily dose for adults is 1 drachm.

Magnesium salicylate $(C_6H_4OHCO_2)_2Mg,4H_2O$. This compound, prepared by the interaction, at high temperatures, of salicylic acid and magnesium carbonate, forms colourless, stable crystals, soluble in water (1 : 10) and in alcohol. The aqueous solution has a sweetish bitter taste, and a distinct acid reaction.

According to Huchard, this substance was an excellent remedy for abdominal typhus, being antiseptic, and more or less aperient, so that the intestines are cleared of infectious matt

He recommended daily doses of 45 grammes to 1½ drachms. Even in cases accompanied by abundant diarrhœa its use was not held to be contraindicated, as slight laxative symptoms appear only when large doses (1½ to 2 drachms) are given.

Mercury salicylate.—See Mercury Compounds.

Quinine salicylate.—White silky needles, sparingly soluble in water, even with the addition of acid, and hence, best given in pills. Recommended against diarrhœa, rheumatic gout, neuralgia, &c., in doses of 2 to 6 grains.

Terpin Hydrate.

This compound, represented by the formula $C_{10}H_{16}(OH)_2,H_2O$, is prepared by the interaction of a mixture of rectified turpentine oil (4 parts), alcohol (of 80° T) (3 parts), and nitric acid (1 part) in shallow porcelain dishes during some days. A crystalline body separates, which is collected, drained, pressed between bibulous paper, and crystallised in the cold from 95 per cent. alcohol made alkaline with a little potash and soda.

Terpin hydrate occurs in large, colourless, and odourless rhombic crystals, with a faint aromatic taste. Soluble in 250 parts of cold (15° C.) or 32 parts of boiling water, in 10 parts of alcohol, 100 of ether, 200 of chloroform, carbon bisulphide, and benzol, but less in turpentine. Melting point 116° to 117° C., with separation of the molecule of water. It should burn away without residue on heating, and should be completely free from odour and from colour.

In small doses (2 to 3 grains) this compound has been credited Manasse and others with the property of increasing the secretion of the bronchial mucous membrane, and when given in larger doses (5 to 6 grains) with stimulating the functional activity of the kidneys. It has, therefore, been given as an expectorant in chronic and subacute bronchitis, and in the treatment of chronic

nephritis. In daily doses of 20 to 40 grains, according to age, it reduces the number of attacks in whooping cough, and promptly cures any co-existent bronchial catarrh (Manasse and Talamon). These effects are probably associated with the antiseptic properties of terpin hydrate. The development of tubercle bacilli is arrested by a 0.25 per cent. solution (Colpi). It has been given in pills (half grain with sugar and gum) in tablets, and in mixture with spirit, syrup, and peppermint water (6 grains to the ounce).

Terpinol is the product obtained by boiling terpin or terpin hydrate with dilute mineral acids; according to Wallach it is a mixture in variable proportions of terpineol ($C_{10}H_{18}O$) and three terpenes: terpinene, terpinolene and dipentene. The substance used by Guelpa and Morra as a bronchial stimulant boiled at 168° C., and was an oily body with a hyacinthine odour, practically insoluble in water, but readily so in alcohol and ether; specific gravity, 0.852. It has been given in daily doses of 8 to 15 grains in capsules or pills.

TABLE I.

Average Doses of New Remedies.

	Pro dosi.	Pro die.
Acetanilid	2— 5 grns.	45 grns.
Agaricin	$\frac{1}{12}$— $\frac{1}{6}$ grn.	1 grn.
Amylene hydrate	45—60 grns.	2 drms.
Anisic acid (sodium salt)	15 grns.	—
Antipyrin	15—30 grns.	—
Benzanilid	15—45 grns.	—
Benzosol	4 grns.	—
Betol	5— 8 grns.	15—30 grns.
Bismuth salicylate ..	10—15 grns.	45 grns.
Bromacetanilid	2— 8 grns.	—
Bromoform	1— 2 ms.	5—20 ms.
Bromol	1 grn.	8 grns.
Chinoline salts	5—20 grns.	—
Chloralamid	30—45 grns.	1½ drms.
Chloralammonium ..	30—45 grns.	1½ drms.
Chloralcyanhydrate ..	⅓ grn.	—
Chloralurethane	10—40 grns.	—
Creolin	5 ms.	—
Creosote	3 ms.	—
Dithiosalicylic acid II. ..	8 grns.	30 grns.
Diuretin	15 grns.	45—90 grns.
Ethyl bromide	5—10 drops.	—
Eucalyptol	5 drops.	—
Euphorine	6— 8 grns.	20—30 grns.
Exalgin	½— 4 grns.	—
Guaiacol	2 ms.	15 ms.
Hydracetin	$\frac{1}{6}$— 1 grn.	2 grns.

TABLE I.—(*continued*).

	Pro dosi.	Pro die.
Hydroquinone	6— 9 grns.	—
Hypnal	15 grns.	—
Hypnone	3— 8 ms.	—
Ichthyol	4—20 ms.	—
Iodol	3 grns.	8—15 grns.
Lithium salicylate.. ..	6—10 grns.	1 drm.
Magnesium salicylate ..	10—20 grns.	45—90 grns.
Mercury, compounds of ..	$\frac{1}{5}$— $\frac{1}{2}$ grn.	2 grns.
Methacetin	5—15 grns.	—
Methylal	15—30 ms.	2 drms.
Methylene blue	$1\frac{1}{2}$— 8 grns.	—
Myrtol	5 ms.	15 ms.
Naphtalene..	1— 2 grns.	8 grns.
Orexin hydrochloride ..	5— 8 grns.	—
Paraldehyde	$\frac{1}{2}$— 1 drm.	—
Phenacetin	8—12 grns.	$1\frac{1}{2}$ drms.
Phenocoll hydrochloride ..	8—15 grns.	$1\frac{1}{2}$ drms.
Piperazine	15 grns.	45 grns.
Quinine salicylate.. ..	2— 5 grns.	15 grns.
Resorcin	3— 8 grns.	45 grns.
Salipyrin	15 grns.	—
Salol	15—30 grns.	2 drms.
Sodio-theobromine salicyl. (*v.* Diuretin)	—	—
Sodium anisate (*v.* Anisic acid)	—	—
Sodium ichthyolsulphonate	3 grns.	10 grns.
,, paracresotate ..	15—30 grns.	—
Somnal	30 ms.	—

TABLE I.—(*continued*).

	Pro dosi.	Pro dosi.
Sulphonal	15—30 grns.	1½ drms.
Terpin hydrate	3—10 grns.	20—40 grns.
Terpinol	2 ms.	8—15 ms.
Tetronal	15—30 grns.	1½ drms.
Thallin salts	2— 5 grns.	—
Thiol (liquid)	4—20 ms.	—
Tribromophenol (*v.* Bromol)	—	—
Trional	15—30 grns.	1½ drms.
Urethane	15—40 grns.	—

Professor Demme, of the Jenner Children's Hospital, Berne, gives the following:—

Dosage of Antipyretics for Children.

	Children of		
	2—4 years.	5—10 years.	11—15 years.
Acetanilid, 1—3 times daily, pro dosi	1—1½ grns.	2— 4 grns.	4— 5 grns.
Antipyrin, 2—3 times daily, pro dosi	3—6 grns.	8—10 grns.	12—15 grns.
Phenacetin, single dose	2—4 grns.	4— 5 grns.	8 grns.
Quinine salts, single dose ..	3—6 grns.	8—10 grns.	10—15 grns.
Salol, 3—4 times daily, pro dosi	4—6 grns.	8—12 grns.	12—15 grns.
Thallin sulphate, every two hours	$\frac{1}{6}$ grn.	$\frac{1}{3}$ grn.	½— 1 grn.

TABLE II.

Solubility of New Remedies in Water and Spirit.

	1 part dissolves in		Remarks.
	Water 15°	Spirit 15°	
Acetanilid	200	10	In about 18 of boiling water or 40 of glycerine. Ph. G. 194 pts. of water and 3½ of alcohol.
Agaricin	little sol.	130	
Amylene hydrate ..	8	freely sol.	Saturated aqueous solutions become turbid when warmed.
Anisic acid	slight.sol.	soluble	
Anthrarobin	inscluble	5	Dissolves in aqueous alkalies, also in glycerine.
Antipyrin	1-	1	
Antisepsin	insoluble	liffc. sol.	
Apyonin	little sol.	freely sol.	
Aristol	insol.	slight.sol.	Taken up by fatty oils by trituration.
Benzanilid	insol.	60	
Benzosol	insol.	sol.	Readily soluble in hot alcohol.
Betol	insol.	diffic. sol.	In about 3 of boiled alcohol.
Bismuth salicyl. ..	insol.	insol.	
Bromacetanilid ..	—	—	v. Antisepsin.
Bromoform	300	freely sol.	
Bromol	prac.insol	freely sol.	Also soluble in ether, chloroform, glycerine and oils.

TABLE II.—*(continued.)*

	1 part dissolves in		Remarks.
	Water 15°	Spirit 15°	
Camphoric acid ..	diffic. sol.	readily sol	Fairly readily soluble in hot water.
Chinoline	prac. insol	5	
— salicyl. ..	80	freely sol.	
— tartrate ..	80	150	
Chloralamid	10	2—3	Is only slowly taken up by water; must not be heated. Chloral-ammonium decomposes even in the cold.
Chloralammonium ..	—	—	
Chloralcyanhydrate	freely sol.	freely sol.	
Chloralimide	insol.	soluble	
Chloralurethane ..	insol.	freely sol.	Decomposes when heated in solution, like all these chloral compounds.
Creolin	—	soluble	Forms emulsion with water.
Creosote	prac. insol	freely sol.	Dissolves in 120 pts. of hot water.
Cresalols	insol.	readily sol	Also taken up by oils.
Cresotic acids	diffic. sol.	readily sol	
Dithiosalicylic acid I.	insol.	insol.	
,, ,, II.	insol.	readily sol	
Diuretin	freely sol.	—	
Ethyl bromide	insol.	soluble	Also miscible with ether chloroform and oils.
Eucalyptol	insol.	freely sol.	
Eucalyntoresorcin ..	insol	soluble	Also soluble in ether and chloroform.

TABLE II.—*(continued.)*

	1 part dissolves in		Remarks.
	Water 15°	Spirit 15°	
Euphorine	insol.	readily sol	Taken up by mixtures of alcohol and water (wines).
Exalgin	diffic. sol.	readily sol	
Fluorescein	soluble	—	
Guaiacol	200	readily sol	
Hydracetin	50	readily sol	Taken up by 8-10 boiling water.
Hydronapthol	little sol.	soluble	
Hydroquinone	readily sol	readily sol	
Hydroxylamine hydro.	1	15	Also in glycerine.
Hypnal	15	—	
Hypnone	insol.	readily sol	Also miscible with fatty oils.
Ichthyol	freely sol.	partly sol.	
Iodantipyrin	diffic. sol.	diffic. sol.	More freely soluble in the hot menstrua.
Iodol	prac. insol	3	Alcohol solutions are precipitated by water, but not by glycerine.
Kairin	6	20	
Lanolin	insol.	80 (78°C.)	Readily miscible with an equal weight of water.
Lithium salicyl. ..	1	—	
Lysol	freely sol.	freely sol.	
Magnesium salicyl.	10	10	
Mercury benzoate ..	prac. insol	diffic. sol.	
— carbolate ..	insol.	v. diffi. sol.	
— glycopeptonate	soluble	soluble	

TABLE II.—*(continued.)*

	1 part dissolves in		Remarks.
	Water 15°	Spirit 15°	
— imidosuccin. . .	25	300	
— naphtolacet. . .	insol.	insol.	
— oxycyanide . .	sol. (?.)	—	
— salicylate . .	insol.	insol.	
— thymolacet. . .	—	soluble	Readily soluble in dilute alkalies.
Metaldehyde	insol.	readily sol	
Methacetin	530	readily sol	Also taken up by glycerine.
Methylal	3	readily sol	Miscible with oils.
Methyl chloride . .	—	—	Water absorbs 4 and alcohol 35 volumes.
Methylene blue . .	slight.sol.	readily sol	
,, chloride . .	slight.sol.	readily sol	
Myrtol	insol.	readily sol	
Naphtol	1000	readily	Solubility in water is increased by the presence of boric acid.
Naphtalene	insol.	diffic. sol	
Orexin hydrochl. . .	freely sol.	freely sol	
Oxynaphtoic acid . .	prac.insol	readily sol	
Paraldehyde	10	readily so	A solution saturated at 15° separates paraldehyde when heated. Ph. G. 8½ pts. of water.
Phenacetin	prac.insol	diffic. sol.	Ph. G. 1,400 pts. of water and 16 pts. of alcohol.
Phenocoll hydrochl.	16	—	

TABLE II.—*(continued.)*

	1 part dissolves in		Remarks.
	Water 15°	Spirit 15°	
Piperazine hydroc.	freely sol.	—	
Pyoctanin, blue ..	50 (?)	—	Generally used in 1 % solutions and upwards.
Pyridin	—	1	Miscible with water in all proportions.
Resopyrin	insol.	soluble	
Resorcin	2	readily sol	Ph. Ger. 1 in 1 of water and 2 in 1 of alcohol.
Saccharin	400	30	
Salipyrin	diffic. sol.	readily sol	
Salol	insol.	10	Alcoholic solutions form emulsions with water.
Sodium anisate ..	readily sol	—	
,, dithiosalicyl.	1	—	
,, paracresot. ..	—	—	Soluble in about 24 parts of warm water.
Sozoiodol	readily sol	readily sol	Also taken up by alcohol.
,, -mercury	500	—	Freely soluble in sod. chlor. solution.
,, -potass. ..	50	—	
,, -sodium ..	14	—	
,, -zinc ..	20	soluble	
Sulphonal	450	65	B.P. Add.; "in about 50 fl. parts of cold rectified spirit."
Terpin hydrate	250	10	Little taken up by oil of turpentine.

TABLE II.—*(continued.)*

	1 part dissolves in		Remarks.
	Water 15°	Spirit 15°	
Terpinol	prac.insol	readily sol	
Tetronal	450	readily sol	
Thalline sulphate ..	7	100	2:1 of boiling water.
— tartrate ..	10	slight.sol.	
Thiol	soluble	soluble	
Thioresorcin		diffic. sol.	
Trional	320	readily sol	
Urethane	1	0.6	

TABLE III.

Melting and boiling points of New Remedies.
in Centigrade degrees.

	M. p.	B. p.	S.g. & Remarks
Acetanilid	114°	295°	B.P. Add: m.p =112.8° C
Agaricin	128°—129°	—	
Amylene hydrate ..	—12°	102.5°	S.g. 0.81
Anisic acid	175°	280°	
Antipyrin	113°	—	B.P. Add: m.p. =110°
Antisepsin	165°	—	
Apyonin	—	—	

TABLE III. (*continued*).

	M. p.	B. p.	S.g. & Remarks
Benzanilid	163°	—	
Benzosol	50°	—	
Betol	95°	—	
Bromoform	4°.5	147°—148°	S.g. 2.9
Bromol	95°	—	
Camphoric acid ..	175°—178°	—	
Chinoline	—	237°	S.g. 1.084
Chloralamid ..	115°	—	
— ammonium ..	62°—64°	—	
— cyanhydrate	—	—	Decomposes when heated
— imide ..	168°C	—	
— urethan ..	100°—103°	—	
Cresalol, ortho ..	35°	—	
— meta ..	74°	—	
— para ..	39°	—	
Cresol, ortho ..	31°	185°—186°	
— meta ..	—	195°—200°	
— para ..	36°	198°	
Cresotic acid, ortho	160°	—	
— meta	177°	—	
— para	151°	—	
Ethyl bromide ..		38°—39°	S.g. 1.38—1.39
Eucalyptol	—1°	176°—177°	S.g. 0.930
Eucalyptoresorcin ..	90°	—	Volatilise and sublime at 100° C.
Euphorin	51°	—	
Exalgin	100°	240°—250°	

TABLE III. (*continued*).

	M. p.	B. p.	S.g. & Remarks
Guaiacol	—	200°—202°	S.g. 1.117
— carboxylate ..	148°—150°	—	
— cinnamate ..	130°	—	
Hydracetin	128°—129°	—	
Hydroquinone ..	172.5°	—	When rapidly heated it decomposes
Hypnal	67°—68°	—	
Hypnone	20.5°	210°	S.g. 1.032
Iodantipyrin ..	160°	—	
Iodol	—	—	Decomposes between 140° and 150°
Lanolin	40°—44°	—	B.P. Add: 37°.8
		—	and 44°.4
Metaldehyde ..	—	—	Sublimes without melting at 112° — 115°, being partly decomposed.
Methacetin	127°		Distil unchanged.
Methylal	—	42°	S.g. 0.855
Methyl chloride ..	—	21°	S.g. 0.9915 (at -23.7° C)
Methylene chloride	—	41°—42°	S.g. 1.354
Myrtol	—	160°—170°	
Naphtol	123°	286°	
Naphtalene	80°	218°	

TABLE III. (*continued*).

	M. p.	B. p.	S.g. & Remarks
Oxynaphtoic acid α-	186°	—	Decomposes as it melts.
Paraldehyde ..	10°	124°	S.g. 0 998
Phenacetin	135°	—	
Phenocoll	115°	—	
Piperazine	104°	145°—146°	
Pyridine	—	117°	S.g. 0.9858 (0°C)
Resopyrin	—	—	"Melts very readily"
Resorcin	118°	276°	Ph. G: melts at 100°—111°
Saccharin	200°	—	Decomposes readily when heated.
Salipyrin	89°—90°	—	Decomposes above 90°
Salol	42°—43°	—	
Sulphonal	125°—126°	—	B.P. Add: 105°5
Terpin hydrate ..	116°—117°	258°	Loses a molecule of water in melting so the M.p. is that of terpin.
Terpinol	—	168°	S g. 0.852
Tetronal	85°	—	
Thallin sulphate ..	100°+	—	Decomposes above the m.p.
Trional	76°	—	
Urethane	47°—50°	170°—180°C	Scarcely decomposes even when boiled.

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TABLE III. (*continued*).

	M. p.	B. p.	S.g. & Remarks
Guaiacol	—	200°—202°	S.g. 1.117
— carboxylate ..	148°—150°	—	
— cinnamate ..	130°	—	
Hydracetin	128°—129°	—	
Hydroquinone ..	172.5°	—	When rapidly heated it decomposes
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Iodol	—	—	Decomposes between 140° and 150°
Lanolin	40°—44°	—	B.P. Add: 37°.8
		—	and 44°.4
Metaldehyde ..	—	—	Sublimes without melting at 112° — 115°, being partly decomposed.
Methacetin	127°		Distil unchanged.
Methylal	—	42°	S.g. 0.855
Methyl chloride ..	—	21°	S.g. 0.9915 (at -23.7° C)
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TABLE III. (*continued*).

	M. p.	B. p.	S.g. & Remarks
Oxynaphtoic acid α-	186°	—	Decomposes as it melts.
Paraldehyde ..	10°	124°	S.g. 0 998
Phenacetin	135°	—	
Phenocoll	115°	—	
Piperazine	104°	145°—146°	
Pyridine	—	117°	S.g. 0.9858 (0°C)
Resopyrin	—	—	"Melts very readily"
Resorcin	118°	276°	Ph. G: melts at 100°—111°
Saccharin	200°	—	Decomposes readily when heated.
Salipyrin	89°—90°	—	Decomposes above 90°
Salol	42°—43°	—	
Sulphonal	125°—126°	—	B.P. Add: 105°5
Terpin hydrate ..	116°—117°	258°	Loses a molecule of water in melting so the M.p. is that of terpin.
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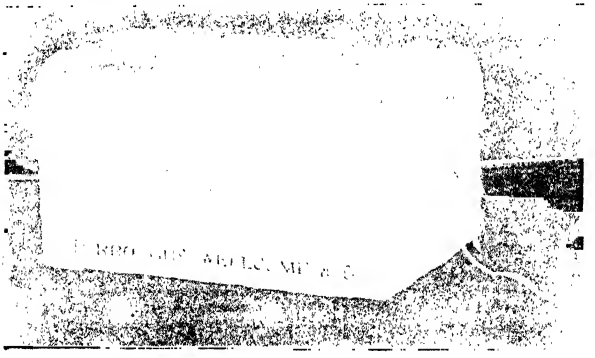

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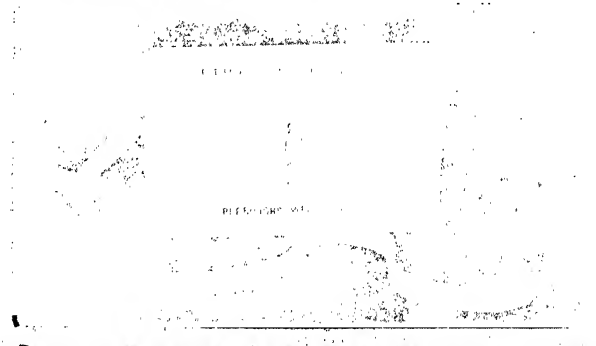

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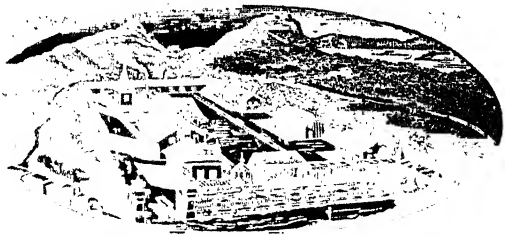

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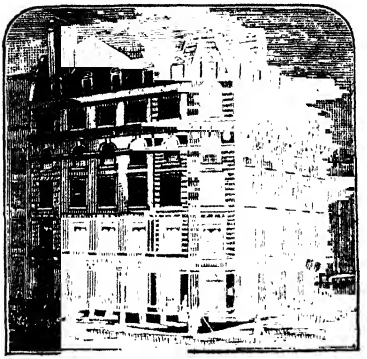

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A. B. Griffiths, Ph.D., F.R.S.E., F.C.S., in his "Researches on Micro-Organisms," writes :—"Hydronaphthol is of great value as an *antiseptic* agent in surgical operations, &c.—A solution 1 to 1,100 destroys *Bacillus subtilis*, *Micrococcus tetragonus*, *Micrococcus, prodigiosus*, *Bacillus anthracis* and its spores, *Sarcina lutea*, and other microbes—for they cannot be cultivated after its action." The minimum antiseptic action of this important compound lies very nearly at 1 in 7,200, while the maximum lies between 1 in 2,500 and 1 in 3,000.

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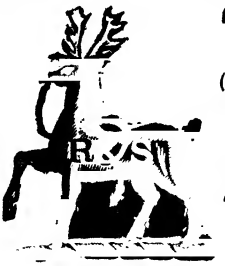

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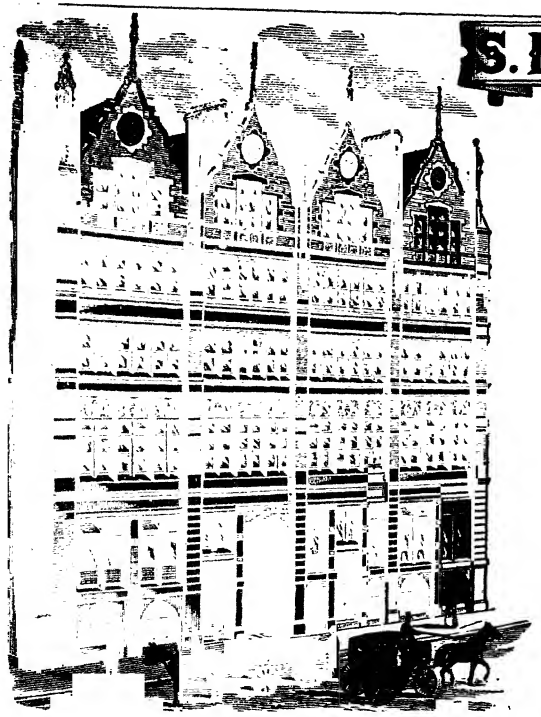

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